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Food and Drug Administration
Department of Health and Human Services
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By Hand

Citizen Petition Seeking Withdrawal of Approvals of Certain Herdwide/Flockwide Uses of Critically and Highly Important Antibiotics Pursuant to Guidance #152

A. Action Requested

On behalf of Environmental Defense, the American Academy of Pediatrics, the American Public Health Association, and the Union of Concerned Scientists (hereinafter referred to as the Petitioners),[1] the undersigned submits this petition[2] under section 512(e) of the Federal Food, Drug, and Cosmetic Act (FDCA) to request the Commissioner to withdraw approvals for herdwide/flockwide uses of the below-listed antibiotics[3] in chicken, swine, and beef cattle for purposes of growth promotion (including weight gain and feed efficiency) and disease prevention and control (except for non-routine use where a bacterial infection has been diagnosed within a herd or flock):

- Penicillins (natural penicillins, penase resistant penicillins,[4] antipseudomonal penicillins, and aminopenicillins)
- Tetracyclines
- Aminoglycosides
- Streptogramins
- Macrolides
- Lincomycin
- Sulfonamides

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[1] See Appendix 1 for descriptions of the Petitioners.

[2] This petition follows the format required by FDA's regulations governing Citizen Petitions. See 21 C.F.R. 10.30. Available at www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=10.30 (accessed Apr. 5, 2005).

[3] While antibiotics are technically a subset of antimicrobials, this petition uses the term "antibiotic" as synonymous with the more technical term "antimicrobial" because the latter is not used in general parlance.

[4] Also referred to as penicillinase-resistant penicillins.

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Specifically, we request that the Commissioner promptly initiate and conclude proceedings to rescind or amend existing approvals covering the drug uses specified in the Addendum to this Petition.[5]

The requested actions are consistent with the criteria set forth in Guidance #152, issued by the Food and Drug Administration (FDA) on October 23, 2003,[6] and with the positions of numerous public health and medical experts. As the first line of the Guidance notes, that document lays out a "recommended approach for assessing the safety" of agricultural antibiotics with regard to antibiotic resistance.

The drugs covered by this Petition meet both of two criteria. First, they are designated (individually or as a member of a drug class) as a "critically important" or "highly important" antibiotic under the Guidance. Second, they are approved for use in chicken, swine, or beef cattle for growth promotion (including weight gain and feed efficiency), disease prevention, or disease control. However, Petitioners do not seek withdrawal of disease prevention or disease control uses where a drug is administered to individual animals, or to select groups or pens of animals,[7] or where a drug is administered in response to a diagnosed outbreak of bacterial disease within a building, house, or feedlot.[8] Insofar as withdrawal of existing approvals would bar uses of these prevention/control uses, Petitioners request that FDA instead amend the approvals to permit *only* disease prevention/control that involves administration to an individual animal, or to select groups or pens of animals, or in response to a diagnosed outbreak of bacterial disease within a building, house, or feedlot. **It is important to note that this Petition does *not* cover any uses of any drugs for disease treatment.**

While the Guidance would encompass additional use restrictions beyond those covered in this Petition, we believe that the Petition covers the most clear-cut examples of inappropriate use on which FDA should take immediate action. This is because the uses covered by the Petition account for the greatest volumes of uses of medically important antibiotics, and because elimination of these uses can most readily be accomplished. Indeed, other nations – notably Denmark, the world's largest exporter of pork – have already done so, and high-volume meat purchasers in the U.S. are increasingly seeking meats produced without routine use of antibiotics (see next section below).

Though not a basis for this petition *per se,* it is noteworthy that FDA has never determined that the existing herdwide/flockwide uses covered by this Petition meet modern scientific standards for safety with regard to antibiotic resistance. These uses

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[5] For some of the drug uses covered by the petition, FDA initiated proceedings in the mid-1970s, but to date has not taken final action with regard to those proceedings and they remain pending. See Appendix 3 and materials cited therein.

[6] Guidance for Industry #152, Guidance on Evaluating the Safety of Antimicrobial New Animal Drugs with regard to their Microbiological Effects on Bacteria of Human Health Concern, Oct. 23, 2003. Available at www.fda.gov/cvm/guidance/fguide152.pdf (accessed Apr. 5, 2005).

[7] The phrase "select groups or pens of animals" is taken from page 23, Table 7 of the Guidance.

[8] The phrase "within a building, house [or] feedlot" is taken from page 23 of the Guidance.

were initially approved decades ago. While FDA requested supplemental data in the 1970s relating to antibiotic resistance, those data were generated using test methods so seriously flawed that even the trade association for the animal-drug industry has recently acknowledged that they "are not predictive."[9] As a senior FDA scientist has observed, "These studies, as designed, are 30 years old. Science has moved on."[10] See Appendix 2.

Moreover, FDA has itself acknowledged that some of the uses covered by this Petition are inconsistent with this Guidance. In May 2004, FDA sent letters to four producers of penicillin feed additives approved for growth-promoting uses (copies of the letters, which were obtained under the Freedom of Information Act, are contained in Appendix 3). Each letter stated in part:

> "The administrative record does not contain sufficient information to alleviate [FDA's] concern about the use of these products and their possible role in the emergence and dissemination of antimicrobial resistance. ... The outcome of the qualitative risk assessment conducted [by FDA] according to Guidance #152 is that the product is considered Category 1 [i.e., high risk]. "

The agency concluded by noting that growth promotion and related uses "are not considered appropriate for Category 1 or 2 products under Guidance #152." Unfortunately, in the ten months since these letters were sent, the manufacturers of these products have failed to comply with FDA's implicit request to voluntarily remove these substances from the market.

B. Statement of Grounds

1. Background: The Emerging Medical Crisis of Antibiotic Resistance and the Agricultural Use of Antibiotics

A number of prominent health-focused institutions have flagged antibiotic resistance as a serious problem for human medicine. The Centers for Disease Control has identified antibiotic resistance as one of its "top concerns."[11] A federal interagency task force including representatives from FDA recently noted that antibiotic resistance is "a growing menace to all people" and that, absent effective action, treatments for common infections "will become increasingly limited and expensive – and, in some cases,

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[9] Animal Health Institute, Alexander S. Mathews, President & CEO. Comments to FDA Docket No. 98D-0969, "FDA Workshop on Pre-Approval Studies in Antimicrobial Resistance and Pathogen Load," May 3, 2000. Available at www.fda.gov/cvm/Documents/VMACAHIComments1..pdf (accessed Apr. 5, 2005).

[10] Remarks of Jean Cooper, FDA, "'558.15' studies: A historical perspective," at FDA public meeting "Pre-Approval Studies in Antimicrobial Resistance and Pathogen Load." (Feb. 22, 2000) (p. 121). Meeting transcript available at www.fda.gov/cvm/Documents/CVM-PSES222.doc (accessed Apr. 5, 2005).

[11] Centers for Disease Control (CDC). Background on Antibiotic Resistance. Atlanta, GA. Available at www.cdc.gov/drugresistance/community (accessed Apr. 5, 2005).

nonexistent."[12] The Infectious Disease Society of America warns that the pipeline of new drugs to combat bacterial diseases is "drying up" even as bacteria are becoming increasingly resistant to existing antibiotics.[13] The new-drug drought reflects in part the fact that it is far more profitable for pharmaceutical companies to develop drugs to treat chronic conditions because a patient must take those drugs for years. By contrast, in most instances a patient need take antibiotics only for a week or so.

In 1998, the National Academy of Sciences stated that antibiotic-resistant bacteria "generate a minimum of $4 billion to $5 billion in costs to U.S. society and individuals yearly."[14] Patients infected with drug-resistant organisms "are more likely to have longer hospital stays and require treatment with second- or third-choice drugs that may be less effective, more toxic, and/or more expensive."[15]

In addition, numerous expert organizations have recognized that, along with medical overuse of antibiotics, agricultural overuse of antibiotics contributes to the development and spread of resistant bacteria, imperiling human health:

- National Academy of Science's Institute of Medicine: "Clearly, a decrease in the inappropriate use of antimicrobials in human medicine alone is not enough. Substantial efforts must be made to decrease inappropriate overuse of antimicrobials in animals and agriculture as well."[16]
- World Health Organization: "There is clear evidence of the human health consequences [from agricultural use of antibiotics, including] infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections."[17]
- Alliance for the Prudent Use of Antibiotics: "the elimination of nontherapeutic use of antimicrobials in food animals and in agriculture will lower the burden of antimicrobial resistance in the environment with consequent benefits to human and animal health."[18]

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[12] Interagency Task Force on Antimicrobial Resistance (undated). A Public Health Action Plan to Combat Antimicrobial Resistance, p. 9. Available at www.cdc.gov/drugresistance/actionplan/aractionplan.pdf (accessed Apr. 5, 2005).
[13] Infectious Diseases Society of America (2004). Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates ... A Public Health Crisis Brews, p. 3. www.idsociety.org/pa/IDSA_Paper4_final_web.pdf (accessed Apr. 5, 2005).
[14] National Academy of Sciences Institute of Medicine (1998). Antimicrobial Resistance: Issues and Options. Washington, DC: National Academies Press, p. 1. Available at http://www.nap.edu/openbook/0309060842/html/1.html#pagetop (accessed Apr. 5, 2005).
[15] Centers for Disease Control, Campaign to Prevent Antimicrobial Resistance in Healthcare Settings: Why a Campaign? www.cdc.gov/drugresistance/healthcare/problem.htm (accessed Apr. 5, 2005).
[16] Institute of Medicine, Board on Global Health (2003). Microbial Threats to Health: Emergence, Detection, and Response. National Academy of Sciences Press, Washington, DC. Available at http://books.nap.edu/books/030908864X/html/207.html#pagetop (accessed Apr. 5, 2005).
[17] Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance (2003), p. 1. www.who.int/foodsafety/publications/micro/en/report.pdf (accessed Apr. 5, 2005).
[18] APUA, The Need to Improve Antimicrobial Use in Agriculture: Ecological and Human Health Consequences. *Clinical Infectious Diseases*, Vol. 34 Supp 3, p. S75 (footnote omitted). Available at www.journals.uchicago.edu/CID/journal/contents/v34nS3.html (accessed Apr. 5, 2005).

In addition, the Department of Health and Human Services has itself noted that "there is a preponderance of evidence that the use of antimicrobials in food-producing animals has adverse human consequences."[19]

Unsurprisingly, the U.S. trade association for producers of agricultural antibiotics, the Animal Health Institute (AHI), opposes restrictions on use of agricultural antibiotics, as do certain meat producers and the American Veterinary Medical Association. As the U.S. General Accounting Office (subsequently renamed the Government Accountability Office) noted in its recent report on agricultural antibiotics, "Many studies have found that the use of antibiotics in animals poses significant risks for human health, but a small number of studies contend that the health risks of the transference are minimal."[20] The latter include a recent review article by Phillips *et al.*[21] In the article, the authors state that they "were initially convened as an advisory board" by AHI and that "We are grateful to AHI who kindly agreed to cover the costs of the preparation of this review: circulation of drafts, acquisition and circulation of references, and production of fair copy based on the drafts."

The Phillips *et al.* article has been sharply criticized by, among others, senior scientific officials at both FDA and CDC. For example, the Deputy Director of FDA's Center for Veterinary Medicine noted that the Phillips article "contains several factual errors" and further noted that their assessment "diverges from the majority of the peer-reviewed scientific literature on the subject, casting doubt on how objectively the authors reviewed the published data. The credibility of the authors' assessment is further strained by frequent improper citation of the published literature."[22] Similarly, CDC scientists noted that Phillips *et al.* had "incorrectly linked these [CDC] studies to statements that do not summarize the conclusions of the authors."[23] Other scientists characterized the article as

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[19] Comments from the Department of Health and Human Services, Appendix VII (p.89) *in* U.S. General Accounting Office (2004), *Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals*. GAO-04-490. Available at www.gao.gov/new.items/d04490.pdf (accessed Apr. 5, 2005).

[20] U.S. General Accounting Office (2004). *"Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals"*, report no. 04-490, unnumbered first page. Available at www.gao.gov/new.items/d04490.pdf (accessed Apr. 5, 2005).

[21] I. Phillips, M. Casewell, T. Cox, B. De Groot, C. Friis, R. Jones, C. Nightingale, R. Preston, and J. Waddell (2004). "Does the Use of Antibiotics in Food Animals Pose a Risk to Human Health? A Critical Review of Published Data," *Journal of Antimicrobial Chemotherapy*, 53: 28-52.

[22] L. Tollefson (2004). "Factual errors in review article," *Journal of Antimicrobial Chemotherapy* 54: 271-271 (footnote omitted). Dr. Tollefson, a veterinarian, is the Deputy Director of FDA's Center for Veterinary Medicine, and holds the rank of Assistant Surgeon General (Rear Admiral). See www.fda.gov/cvm/CVM_Updates/tollpromo.htm (accessed Apr. 5, 2005).

[23] T.M. Chiller, T. Barrett and F. J. Angulo (2004). "CDC studies incorrectly summarized in 'critical review'," *Journal of Antimicrobial Chemotherapy*, 54: 275-276. Dr. Chiller is Chief of the NARMS (National Antimicrobial Resistance Monitoring Systems) Unit at CDC. Dr. Barrett is Chief of CDC's FoodNet and NARMS Laboratory. Dr. Angulo, who holds both a DMV and an Ph.D. in epidemiology, is Chief of CDC's FoodNet and NARMS Unit. See www.cdc.gov/narms/staff.htm (accessed Apr. 5, 2005).

"fraught with inaccurate and misleading citations and other errors,"[24] and pointed to instances of "misquoting and misinterpreting scientific results."[25] Consistent with its usual practice, GAO requested comments on a prior draft of the report from relevant federal agencies, including the Department of Health and Human Services; HHS's comments included the statement that "We believe GAO should note in its report that the article they cite [i.e., Phillips *et al.*] was written by an advisory group to the Animal Health Institute."[26]

In addition, HHS's comments on the GAO report summarize recent scientific literature indicating that the very bacteria that are resistant may also be more virulent:[27] "In a prospective CDC study of 758 salmonellosis cases, patients with resistant infections were significantly more likely [to] be hospitalized than were those with susceptible infections, even after accounting for underlying illness and prior antimicrobial exposure using multivariate techniques." In addition, the comments described studies showing substantially increased mortality in the two years following infection with resistant S. Typhimurium compared to susceptible S. Typhimurium, and similar results for resistant versus susceptible *Campylobacter* infections.

Recent research also indicates that resistant foodborne bacteria are associated with ailments not traditionally regarded as foodborne illnesses, namely urinary tract infections (UTIs). As the authors of the most recent study noted, "The possibility that human drug-resistant UTI could be a foodborne illness has serious public health implications."[28]

2. The Development of Guidance #152

As detailed in Part III of this Petition, the actions requested herein are consistent with FDA's Guidance #152. As FDA noted in releasing the Guidance, that document "outlines a comprehensive evidence-based approach to preventing antimicrobial resistance that may result from the use of antimicrobial drugs in animals."[29] The Guidance reflects

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[24] B.E. Karp and J.Engberg (2004). "Comment on: Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data," *Journal of Antimicrobial Chemotherapy,* 54(1): 273-274. Dr. Karp is a Veterinary Medical Officer in the Division of Epidemiology at FDA's Center for Veterinary Medicine. See http://www.fda.gov/cvm/cvmlist4.html (accessed Apr. 5, 2005).

[25] V.F. Jensen, J. Neimann, A.M. Hammerum, K. Mølbak, and H.C. Wegener (2004). "Does the use of antibiotics in food animals pose a risk to human health? An unbiased review?," *Journal of Antimicrobial Chemotherapy,* 54(1): 274-275. The authors are scientists with the Danish Institute for Food and Veterinary Research and the Statens Serum Institut.

[26] GAO Report no. 04-490, p. 89, www.gao.gov/new.items/d04490.pdf.

[27] Ibid., p. 90.

[28] M. Ramchandani, A.R. Manges, C. DebRoy, S.P. Smith, J.R. Johnson, and L.W. Riley (2005). "Possible Animal Origin of Human-Associated, Multidrug-Resistant, Uropathogenic Escherichia coli." Clinical Infectious Diseases 40: 251-257. Available at www.journals.uchicago.edu/CID/journal/issues/v40n2/34442/brief/34442.abstract.html (accessed Apr. 5, 2005).

[29] FDA, "FDA Issues Guidance on Evaluating the Safety of Antimicrobial New Animal Drugs to Help Prevent Creating New Resistant Bacteria" (press release), Oct. 23, 2003. Available at www.fda.gov/bbs/topics/NEWS/2003/NEW00964.html (accessed Apr. 5, 2005).

the results of a careful deliberative process lasting nearly five years. During that period, FDA held numerous public meetings, proposed two earlier approaches for evaluating agricultural antibiotics (the "Framework"[30] document and the "Thresholds"[31] document), and developed a prior draft of the Guidance.[32] In addition, FDA held multiple public meetings and also solicited (and received) public comment. The final Guidance is thus the result of a procedure that has involved extensive public as well as agency involvement over several years.

Issuance of the final Guidance was hailed both by industry and advocates. For example, a press release issued by the Animal Health Institute was headlined "Industry Welcomes New FDA Guidance on Antibiotics," and noted that "This is the culmination of a process that has dragged on nearly five years."[33] AHI further lauded the guidance as a "risk-based approach" that "will allow FDA to make sound management decisions." Similarly, Keep Antibiotics Working's press release "applauded" release of the Guidance (though noting with dismay the absence of a schedule for taking action with regard to already-approved antibiotics).[34]

3. Legal Standard for Withdrawal of Animal Drugs

a. The Standards of FDCA Section 512 and Guidance #152

Animal drugs can only be marketed if approved by FDA under section 512 of the Food Drug and Cosmetics Act; FDA's mechanism for granting such approvals is termed a "new animal drug application," or NADA. Somewhat confusingly, all animal drugs now on the market are thus termed "new animal drugs," even though many have been on the market for decades.

Section 512 specifies that a NADA must be denied if the Secretary of Health and Human Services finds that available data show that a drug is **"unsafe"** for use under the proposed use conditions or the data **"do not show that such drug is safe"** under such

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[30] FDA Docket No. 98D-1146 - Discussion Paper: "A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals." (64 Fed. Reg. 887, Jan. 6, 1999). Available at www.fda.gov/cvm/VMAC/antimi18.html (accessed Apr. 5, 2005).

[31] "An Approach for Establishing Thresholds in Association with the Use of Antimicrobial Drugs in Food-Producing Animals" (Dec. 19, 2000). Available at www.fda.gov/cvm/Documents/threshold21.pdf (accessed Apr. 5, 2005).

[32] FDA, "Draft Guidance for Industry: Evaluating the Safety of Antimicrobial New Animal Drugs With Regard to Their Microbiological Effects on Bacteria of Human Health Concern," 67 Fed. Reg. 58058-58060 (Sept. 13, 2002). Available at www.fda.gov/OHRMS/DOCKETS/98fr/98d-1146-gdl0001.doc (accessed Apr. 5, 2005).

[33] Animal Health Institute Press Release, Oct. 23, 2003. Available at www.ahi.org/mediaCenter/documents/Guidance152.pdf (accessed Apr. 5, 2005).

[34] Keep Antibiotics Working Press Release, Oct. 23, 2003. Available at www.iatp.org/antibiotics/library/uploadedfiles/KAW_Applauds_FDA_Issuance_of_Final_Guidance_Bu.pdf (accessed Apr. 5, 2005).

conditions;[35] the NADA must also be denied if the Secretary finds that there is "insufficient information to determine whether such drug is safe for use under such conditions."[36] Section 512 also lays out the conditions under which a previously granted NADA is to be withdrawn, i.e., if the Secretary finds that the drug is "**unsafe**" for use under the approved conditions, or if evidence "**shows that such drug is not shown to be safe**" for such use.[37]

Thus, the legal and public health standard for granting and withdrawing NADA approvals are substantively identical, i.e., if a use is either shown to be "unsafe" or is "not shown to be safe."

In Guidance #152, FDA states that it considers an agricultural antibiotic to be "safe" if the agency "concludes that there is reasonable certainty of no harm to human health from the proposed use of the drug in food-producing animals." While Guidance #152 was initially directed at drug producers seeking approval to market additional drugs, the Guidance's criteria apply equally to existing NADAs for drugs now on the market, given that there is no scientific or legal distinction between standards for approval and standards for withdrawal.

As a practical matter, in withdrawing a drug FDA must "provide a reasonable basis from which serious questions about the ultimate safety [of a drug] may be inferred."[38] Such questions "can be raised where the evidence is not conclusive, but merely suggestive of an adverse effect."[39] Once an initial showing of "serious questions" is made, the burden shifts to the drug manufacturer to establish that the use in question is "shown to be safe."[40]

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[35] FDCA § 512(d)(1)(A) & (B), 21 U.S.C. § 360b(d).

[36] FDCA § 512(d)(1)(D), 21 U.S.C. § 360b(d).

[37] FDCA § 512(e), 21 U.S.C. § 360b(e) (emphasis added). Implementing regulations parallel the language of the statute. 21 C.F.R. § 514.115(b). The relevant text of section 512(e) reads as follows:

> (1) The Secretary shall, after due notice and opportunity for a hearing to the applicant, issue an order withdrawing approval of an application filed pursuant to subsection (b) of this section with respect to any new animal drug if the Secretary finds—
> (A) that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved ...;
> (B) that new evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved
> ....

[38] Proposal to Withdraw Approval of the New Animal Drug Application for Enrofloxacin for Poultry, docket no. 00N-1571. Initial Decision of March 16, 2004, at p. 5. Available at www.fda.gov/ohrms/dockets/dailys/04/mar04/031604/00n-1571-idf0001-vol389.pdf (accessed Apr. 5, 2005). Fluoroquinolones are **not** approved for use as feed additives, and this Petition **does not** cover use of fluoroquinolones.

[39] Ibid., p. 5 (embedded quotation marks and citations omitted).

[40] Ibid., p. 7.

b. The Criteria in Guidance #152 Are Applicable to Existing Approvals for Agricultural Antibiotics Now on the Market

As FDA noted in its Press Release on Guidance #152, the Guidance is "the first [document] that addresses, in a comprehensive manner, the issue of the use of antimicrobials in food producing animals as a contributing factor to the development of antimicrobial resistance."[41] Although the Guidance on its face applies only to *future* applications for approval of antimicrobials rather than to drugs already on the market, the 2003 Annual Report for FDA's Center for Veterinary Medicine states that the Guidance's "principles will also be applied in determining whether to remove approved products from the market."[42] In addition, FDA's Federal Register notice for the Guidance states "The guidance represents the agency's current thinking about the safety of [agricultural-animal] drugs, with regard to their microbiological effects on bacteria of human health concern."[43]

As demonstrated in the following section of this Petition, applying the Guidance's criteria to the petitioned drug uses indicates that those uses are inconsistent with the Guidance. As a result, "serious questions" clearly exist with regard to the safety of these uses. Accordingly, FDA should promptly initiate and conclude the process of withdrawing those uses.[44]

4. The Antibiotic Uses Covered by this Petition Are Not Consistent with the Criteria in Guidance #152

Format Note: The following discussion includes several excerpts of tables that are taken verbatim from Guidance #152. Those excerpts are shown in this typeface. The excerpts are identical to the Guidance except as noted by use of brackets; in addition, some footnotes have been omitted.

a. Overview

Guidance #152 lays out FDA's recommended approach to evaluating the safety of agricultural antibiotics with regard to creation of antibiotic-resistant bacteria of human health concern. Although the Guidance in several places uses terms such as "suggested" or "examples" of approaches, this Petition focuses on the substantive content of the

[41] FDA, "FDA Issues Guidance on Evaluating the Safety of Antimicrobial New Animal Drugs to Help Prevent Creating New Resistant Bacteria" (press release), Oct. 23, 2003. Available at www.fda.gov/bbs/topics/NEWS/2003/NEW00964.html (accessed Apr. 5, 2005).

[42] U.S. Department of Health and Human Services, Food and Drug Administration, Center for Veterinary Medicine. Annual Report – Fiscal Year 2003 (October 1, 2002 - September 30, 2003), p. 20. Available at www.fda.gov/cvm/Documents/CVMFY03AnnRpt.pdf (accessed Apr. 5, 2005).

[43] 68 Fed. Reg. 61221 (Oct. 27, 2003). Available at www.fda.gov/OHRMS/DOCKETS/98fr/03-27113.pdf (accessed Apr. 5, 2005).

[44] As noted above, withdrawals for certain uses of some drugs were initiated in the 1970s and remain pending. See Appendix 3.

Guidance, as indicating FDA's best thinking on how these analyses should be performed, and on how identified risks should be managed to avoid unsafe outcomes.

Under the Guidance, use of a particular drug is assigned an overall "risk estimate" of High, Medium, or Low based on a qualitative risk assessment that has three components: release, exposure, and consequence.

- Release. How likely is the drug to be used in food animals in a way that engenders resistance?
- Exposure. How likely are the resistant organisms to make their way to humans?
- Consequence. How important are the drugs for human medicine?

In addition, the Guidance lays out a mechanism for integrating the results of these three assessments into an overall qualitative risk estimate of High, Medium, or Low.

The Guidance also describes risk management steps associated with high, medium, and low risks findings. Among others, these risk management steps include limitations on the extent of use (e.g., individual animal vs. herdwide/flockwide use).

Because this Petition addresses certain already-approved uses, it is convenient to start by considering the Guidance's risk management strategies, before examining the components of the qualitative risk analysis. The following section presents an analysis of these provisions for the uses covered by this Petition.

b. Guidance #152 Allows Herdwide/Flockwide Use Only for "Low Risk" Antibiotics

Table 7 (p. 23) describes high "extent of use" as all flock-wide and herd-wide use, regardless of duration:

Table 7 (excerpt)

Duration of use	Intended administration to: individual animals	select groups or pens of animals	flocks or herds of animals
Short (<6 days)	L[1]	M[2]	H[3]
Medium (6-21 days)	L	M	H
Long (>21 days)	M	H	H

[1]Low, [2]Medium, and [3]High extent of use

Next, Table 8 (p. 25) indicates that a "high" extent of use is *only* allowable for drugs that fall in Category 3 because they have a Low risk ranking; by contrast, "high" extent of use is *not* allowable for drugs in either Category 1 (High risk) or Category 2 (Medium risk):

Table 8 (excerpt)

Approval conditions	Category 1 (High)	Category 2(Medium)	Category 3 (Low)
Extent of use[2]	Low	Low, medium	Low, medium, high

[2]See Table 7 for characterization of extent of use

In summary, herdwide/flockwide use is allowable *only* for drugs with a Low risk ranking. As shown in the following section, the drugs covered by this Petition are not Low risk. Accordingly, their flock- or herd-wide use is inconsistent with the Guidance's safety criteria.

c. The Antibiotics Covered by the Petition are Not "Low Risk"

Under the Guidance, a Low risk ranking occurs *only* under certain circumstances. As noted above, risk rankings are produced by integrating three separate qualitative assessments – "Release," "Exposure," and "Consequence." "Consequence" means the importance of the drug in human medicine, and may be rated as Important, Highly Important, or Critically Important. As further discussed below, "Exposure" describes the likelihood of people to be exposed to antibiotic-resistant bacteria from food, and is rated as High, Medium, or Low; "Release" involves whether agricultural use of the drug selects for resistant bacteria in the animal, and is also rated as High, Medium, or Low.

As shown below, the Release evaluation does not affect the overall Risk ranking for the drugs and uses covered by this Petition; in other words, the Consequence and Exposure evaluations alone will determine the outcome. To demonstrate this, it is useful to look first at the Consequence evaluation, then the Exposure evaluation, and then to consider how the two combine for the final Risk rating.

The Guidance defines drugs' importance in human medicine as "critically" or "highly" important as follows (Table A1, pp. 30-33):

> **Critically Important:** Antimicrobial drugs which meet BOTH criteria 1 and 2 below.
> **Highly Important:** Antimicrobial drugs which meet EITHER criteria 1 or 2 below.
>
> 1. ***Antimicrobial drugs used to treat enteric [gut] pathogens that cause food-borne disease.***

2. *Sole therapy or one of few alternatives to treat serious human disease or drug is essential component among many antimicrobials in treatment of human disease.*[45]

As shown in the following excerpt from the Guidance, the drugs covered by this petition all are ranked as "critically important" or "highly important." Specifically, macrolides are "critically important," while penicillins, aminoglycosides, clindamycin/lincomycin,[46] tetracyclines, glycopeptides, and streptogramins are "highly important." One sulfonamide combination drug – namely trimethoprin/sulfamethoaxole[47] – is also designated as critically important (see discussion in section IV.C. below).

Table A1 (excerpt)

	Classification	1) Enteric pathogen responsible for food-born disease	2) Sole/limited therapy or essential therapy for serious disease (See "Comments" for examples)	3) Used to treat enteric pathogens in non-food-borne disease	4) No cross-resistance within class/no linked cross-resistance with other classes	5) Limited risk of transmission of resistance elements within/across species of organisms	Comments
Natural penicillins	H		X				Neurosyphilis: Serious infection due to Group A streptococci
Benzathine pen G							
Penicillin G							
Penicillin V							
Penase Resistant Pens	H		X				Serious infections due to *Staphylococcus aureus*
Cloxacillin							
Dicloxacillin							
Nafcillin							
Oxacillin							
Antipseudomonal Pens	H		X	X			Serious infections due to *Pseudomonas aeruginosa*
Mezlocillin							
Pipercillin							
Pipercillin/tazo							
Ticarcillin							
Ticarcillin/Clav							

[45] In Petitioners' view, this criterion is insufficiently protective of the public health, inasmuch as it fails to protect valuable drugs simply because there are more than a "few" alternative drugs at present. Given that resistance to existing antibiotics is spreading far more rapidly than new drugs are being developed, this approach is unwise. For purposes of this Petition, however, we employ the Guidance's categorization of drugs.

[46] Table A1 lists clindamycin, which is essentially identical to lincomycin. Clindamycin is the primary form of the drug used in humans, while lincomycin is primarily used in animals. The two drugs differ by a single group: a hydroxyl group (OH) in lincomycin is substituted by a chlorine (Cl) in clindamycin. See "Antimicrobial Chemotherapy," www.bmb.leeds.ac.uk/mbiology/ug/ugteach/icu8/antibiotics/protein.html (accessed Apr. 5, 2005).

[47] Guidance #152 uses the abbreviation "trimeth/sulfameth." See Table A1.

Carbenicillin							
Aminopenicillins	H		X	X			Infections due to *Listeria monocytogenes*
Amoxicillin							
Ampicillin							
Ampicillin/Sulbacta							
Aminoglycosides	H		X	X			
Amikacin							
Gentamicin							Enterococcal endocarditis
Tobramycin							Sole antimicrobial approved for aerosolized therapy in cystic fibrosis
Kanamycin							
Streptomycin							Infections due to *Mycobacterium tuberculosis*
Neomycin							
Netilmicin							
Spectinomycin							Infections due to *Neisseria gonorrhoeae* in pregnancy
Macrolides	C	X	X				Legionnaire's disease: MAC/MAI prophylaxis and therapy
Erythromycin							
Azithromycin							
Clarithromycin							
Clindamycin [Lincomycin]	H		X				Serious infections due to Group A streptococci: Alternative therapy of infections due to *Staphylococcus aureus* in patients with serious beta lactam allergy
Tetracyclines	H		X				Rickettsial disease: Anthrax therapy/prophylaxis
Tetracycline							
Chlorteracycline							
Demeclocycline							
Doxycycline							
Minocycline							
Glycopeptides	H		X				Infections due to methicillin resistant *Staphylococcus aureus*
Vancomycin							
Streptogramins	H		X				Infections due to vancomycin resistant *Enterococcus faecium*
Dalfopristin/quinupristin							
Trimeth/Sulfameth	C	X	X	X			Infection due to *Pneumocystis carinii*

The next key factor is found in Table 6 of the Guidance (p. 21), which provides a grid of all possible combinations of the three assessments' ratings and the resulting risk ranking. Significantly, Table 6 indicates that Critically Important drugs *never* receive a Low risk

ranking, while Highly Important drugs receive a Low risk ranking *if and only if* the Exposure and Release rankings are *both* Low.

Table 6 (excerpt)

Release	***Exposure***	***Consequence***	***Risk Estimation***
Low	Low	Highly important	Low
[Medium or High]	[Medium or High]	Highly important	[Medium or High]
[any]	[any]	Critically Important	[Medium or High]

The Exposure rating is a function of two factors: level-of-consumption and extent-of-contamination (p. 19).[48] Table 2 (p. 17) indicates that consumption of beef, chicken, and pork qualifies as a "High" consumption commodity:

Table 2 (excerpt)

Commodity	***Per capita* consumption (pounds per capita per year)**	**Qualitative ranking**
Beef	62.9	High
Chicken	53.9	High
Pork	46.7	High

The probability of exposure is then determined from Table 5. Under Table 5, if the amount of a food commodity consumed is High, the probability of exposure is always High or Medium (never Low), regardless of extent of contamination of the food commodity:

Table 5

	Probability of human exposure to a given bacteria		
	Amount of food commodity being consumed		
Amount of food commodity contamination	**High**	**Medium**	**Low**
High	H	H	M
Medium	H	M	L
Low	M	L	L

[48] The Guidance's exposure evaluation ignores all non-food pathways, though the Guidance notes in passing that "uncertainties regarding the contribution of other exposure pathways may be considered during the development of appropriate risk management strategies" (p. 15). The Petitioners view the disregard of non-food pathways as another way in which the Guidance is less-than-protective of public health. For purposes of this Petition, however, we employ the Guidance's exposure evaluation scheme, because the uses covered by this Petition are nonetheless inconsistent with even those less-than-protective criteria.

In other words, as a result of the "high" consumption rankings for beef, chicken and pork, the Exposure assessment from Table 5 *never* yields an Exposure ranking of Low. Accordingly, Table 6 shows that there is *no circumstance* that results in an overall Risk estimate of Low for any Highly Important drug.

Critically, because use of the drugs covered by this Petition in chicken, swine, or beef cattle *always* results in a High (Category 1) or Medium (Category 2) risk ranking, "high extent" uses of those drugs – which includes the herdwide/flockwide uses covered by this Petition – are not consistent with the risk management criteria set forth in the Guidance. As noted above and reiterated below, Table 8 (p. 25) indicates that a "high" extent of use is *only* allowable for drugs that fall in Category 3 because of having a Low risk ranking; by contrast, "high" extent of use is *not* allowable for drugs in either Category 1 (High risk) or Category 2 (Medium risk):

Table 8 (excerpt)

Approval conditions	Category 1 (High)	Category 2(Medium)	Category 3 (Low)
Extent of use[2]	Low	Low, medium	Low, medium, high

[2]See Table 7 for characterization of extent of use

d. The Status of Sulfonamides Under Guidance #152

Table A1 does not expressly list sulfonamides, but lists one specific member of the sulfonamides class – trimeth/sulfameth, which is ranked as "critically important." Because other members of the sulfonamides class may cause cross-resistance to trimeth/sulfameth (a combination drug that works synergistically), FDA should also initiate and conclude proceedings to withdraw herdwide/flockwide uses of sulfonamides for growth promotion (including weight gain and feed efficiency) and disease prevention and control (except for non-routine use where a bacterial infection has been diagnosed within a herd or flock) in chicken, swine, and beef cattle. FDA should evaluate all sulfonamides as "critically important" drugs for purposes of the Consequence assessment, and proceed to withdraw approvals for their use as described above absent persuasive evidence showing a lack of cross-resistance to trimeth/sulfameth.

e. Conclusion

In sum, the Petition is entirely consistent with the criteria in Guidance #152 in seeking the withdrawal of approvals for herdwide/flockwide uses of Critically Important and Highly Important antibiotics in chicken, swine, and beef cattle. Because herdwide/flockwide uses for growth promotion and routine disease prevention account for the preponderance of antibiotic use,[49] and because development of resistance is, in

[49] Mellon M, Benbrook C, Benbrook K. 2000. Hogging It!: Estimates of Antimicrobial Abuse in Livestock. Cambridge, MA: Union of Concerned Scientists. Available at www.ucsusa.org/food_and_environment/antibiotic_resistance/page.cfm?pageID=264 (accessed Apr. 5, 2005).

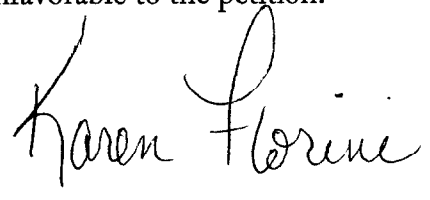
part, a function of the quantity of antibiotics used, FDA should promptly initiate and conclude withdrawals for herdwide/flockwide uses of critically and highly important antibiotics for growth promotion (including weight gain and feed efficiency) and disease prevention and control (except for non-routine use where a bacterial infection has been diagnosed within a herd or flock).

C. Environmental Impact

FDA's regulations indicate that withdrawals of drug approvals are among the class of actions that are "categorically excluded and, therefore, ordinarily do not require the preparation of an EA or an EIS." 21 C.F.R. 25.33 & subsection (g).

D. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



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fax: 202/234-6049
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On behalf of petitioners Environmental Defense, American Academy of Pediatrics, American Public Health Association, Food Animal Concerns Trust, and Union of Concerned Scientists.

Appendix 1: Description of the Petitioners

Environmental Defense is dedicated to protecting the environmental rights of all people, including the right to clean air, clean water, healthy food, and flourishing ecosystems. From its founding in 1967, Environmental Defense has used an innovative mix of scientists, economists, and attorneys to devise practical solutions to environmental problems.

Founded in 1930, the **American Academy of Pediatrics** is an organization of 60,000 pediatricians committed to the attainment of optimal physical, mental, and social health and well-being for all infants, children, adolescents and young adults.

The **American Public Health Association** (APHA) is the oldest organization of public health professionals in the world, representing members from over 50 occupations of public health. APHA has been influencing policies and setting priorities in public health for over 125 years.

Founded in 1982, **Food Animal Concerns Trust** (FACT) advocates for farming practices that improve the safety of meat, milk, and eggs. FACT works to accomplish its goals through on-farm research projects, work with the federal regulatory agencies and Congress, and an ongoing review of the scientific literature.

Founded in 1969, **Union of Concerned Scientists** (UCS) is a non-profit partnership of scientists and citizens combining rigorous scientific analysis, innovative policy development, and effective citizen advocacy to achieve practical environmental solutions.

Appendix 2: FDA Has Not Previously Determined that the Antibiotics Covered By this Petition Meet Modern Scientific Standards for Safety with regard to Antibiotic Resistance.

When approvals for the antibiotic uses covered by this Petition were initially approved decades ago, FDA gave little consideration to safety issues involving antibiotic resistance.[50] In 1973, FDA issued regulations requiring antibiotics already on the market to undergo certain studies.[51] These became known as the 558 studies, because the requirements were codified in section 558 of Part 21 of the Code of Federal Regulations.[52]

However, there were major scientific flaws in the basic protocols for the required studies.[53] The Animal Health Institute (AHI), the trade association for animal-drug

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[50] Indeed, it is not entirely clear exactly how those approvals were issued. As FDA has noted, "Under Section 108 of [the Animal Drug Amendments of 1968], any product that had been approved before 1968 ... would be considered to be the subject of an approved new animal drug application under the new section 512. ... The approval processes for these products before the 1968 amendments were complex, redundant, and involved the acceptance of secondary manufacturers/distributors, sometimes based on a demonstration of equivalence of their products to primary sponsor products and sometimes not. Unlike the current new animal drug application process under section 512 of the act, this was generally not an orderly process. As a result, the agency's and sponsors' ability to document the pre-1968 approvals has been hampered." FDA, Proposed Regulation: New Animal Drugs; Removal of Obsolete and Redundant Regulations [21 CFR 510 and 558]. 68 Fed. Reg. 47272-47277 (Aug. 8, 2003). Available at http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/2003/03-20244.htm (accessed Apr. 5, 2005).

[51] 38 Fed. Reg. 9811 (April 20, 1973) (final rule). The proposed rule had been proposed a year earlier (37 Fed. Reg. 2444) (Feb. 1, 1972). FDA subsequently withdrew approvals for some drugs determined not to be in compliance with the data submission requirements of Sec. 558.15, at 41 Fed. Reg. 8282 (Feb. 25, 1976)). See 68 Fed. Reg. 47273 for a description of the history of Section 558.15.

[52] The regulations were initially codified at 21 CFR 135.109, but were recodified at 21 CFR 558.15 in 1974.

[53] Bacteria are classified as either gram-positive or gram-negative, based on their appearance under the microscope after a certain stain is applied. Gram-positive bacteria are generally killed by a different set of antibiotics than are gram-negative bacteria. Donna U. Vogt and Brian A. Jacson, Congressional Research Service. "Antimicrobial Resistance: An Emerging Public Health Issue." (Jan. 24, 2001) (pp. 3-4, note 9). The 558 studies tested whether certain antibiotics increased the resistance of the gram-negative bacteria *salmonella* and *E. coli* to a range of human-use antibiotics. However, 42 of the 44 drugs tested under this regime were drugs intended to treat gram-positive bacteria, resulting in "a mismatch between the drugs and the bugs." Remarks of Jean Cooper, "'558.15' studies: A historical perspective," at FDA public meeting "Pre-Approval Studies in Antimicrobial Resistance and Pathogen Load." (Feb. 22, 2000) (p. 121). Meeting transcript available at www.fda.gov/cvm/Documents/CVM-PSES222.doc (accessed Apr. 5, 2005). As noted in the meeting transcript (p. 104), Dr. Cooper had previously been with the Center for Veterinary Medicine, but at the time of the meeting was Chief, Clinical Chemistry and Toxicology Branch, Centers for Devices in Radiological Health, FDA.

manufacturers, noted as much in summarizing the views of a public meeting on the 558 protocols:

> "There was consensus that *in vivo* models, at least by current scientific knowledge, were **not considered of value** in predicting the rate and extent of resistance development and the impact this might have on public health....
>
> "It was clearly concluded from the discussions at the workshop that **such studies are not predictive** ... AHI agrees with the conclusions of the workshop."[54]

As an FDA senior staffer put it, "These studies, as designed, are 30 years old. Science has moved on."[55]

In 2003, FDA proposed to repeal the portions of the section 558 regulations relating to these studies on the ground that they were "obsolete" and that "FDA has a new strategy and concept for assessing the safety of antimicrobial new animal drugs, including subtherapeutic use of antimicrobials in animal feed, with regard to their microbiological effects on bacteria of human health concern."[56]

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[54] Animal Health Institute, Alexander S. Mathews, President & CEO. Comments to FDA Docket No. 98D-0969, "FDA Workshop on Pre-Approval Studies in Antimicrobial Resistance and Pathogen Load," May 3, 2000. Available at www.fda.gov/cvm/Documents/VMACAHIComments1..pdf (accessed Apr. 5, 2005).

[55] J. Cooper, "'558.15' studies: A historical perspective," p. 119. Available at www.fda.gov/cvm/Documents/CVM-PSES222.doc (accessed Apr. 5, 2005).

[56] FDA, Proposed Regulation: New Animal Drugs; Removal of Obsolete and Redundant Regulations [21 CFR 510 and 558]. 68 Fed. Reg. 47272-47277, 47276 (Aug. 8, 2003). Available at http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/2003/03-20244.htm (accessed Apr. 5, 2005).

Appendix 3.
Letters from FDA to Manufacturers of Certain Antibiotic Feed Additives.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 26 2004

Carol A. Wrenn
President, Animal Health Division
Alpharma Inc.
One Executive Drive
Fort Lee, New Jersey 07027-1298

Dear Ms. Wrenn:

As you are aware, the Center for Veterinary Medicine was charged with examining previously approved antimicrobial products as a result of an amendment to the FY 2001 appropriations sponsored by U.S. Representative Sherrod Brown. As part of that effort, we have completed our review of the administrative file for your Penicillin 100 (penicillin G procaine 50, Type A Medicated Article, NADA 046-666).

Our review included an examination of the correspondence contained in, data submitted to, and master files referenced in, the administrative file. We conducted a qualitative risk assessment in light of the Center's recently published Guidance for Industry #152 entitled, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," using the information contained in the records.

We are taking this opportunity to provide you with a summary of our findings:

- The codified indications are: ""For increased rate of weight gain and improved feed efficiency."
- §558.15 studies were conducted in swine and chickens. Originally the company participated in the AHI effort and sought subtherapeutic indication. Then the original sponsor withdrew from AHI and sought therapeutic indication.
- CVM reviewed the studies and concluded that they had met the *Salmonella* shedding requirements under §558.15, but that there were still questions about the observed increases in resistant *Salmonella* and *E. coli.* Insufficient information to address GFI #152.
- CVM concluded numerous times that efficacy data were insufficient for the therapeutic claims.
- The NADA was DESI finalized on April 10, 1998 for the subtherapeutic indications.
- CVM's proposal to withdraw penicillin premixes remains pending. 42 FR 43,770. Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

The administrative record does not contain sufficient information to alleviate the Center's concern about the use of your product and its possible role in the emergence and dissemination of antimicrobial resistance. We used only that information on penicillin contained in your administrative file to evaluate your product. Where information on your specific product was lacking, we generally took a conservative approach and assessed the risk as high. The outcome of the qualitative risk assessment conducted according to Guidance #152 is that the product is considered Category 1. Production claims for increased rate of weight gain and improved feed efficiency are not considered appropriate for Category 1 or 2 products under Guidance #152.

The Center for Veterinary Medicine would like to invite you to meet with us and discuss our findings. Please contact my office as soon as possible to arrange this. If you have any questions please contact Dr. Linda Tollefson, Deputy Director at 301-827-2950.

Sincerely yours,

Stephen F. Sundlof, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

cc: NADA 046-666
Director, Office of New Animal Drug Evaluation
Division Director, Human Food Safety

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 26 2004

Carol A. Wrenn
President, Animal Health Division
Alpharma Inc.
One Executive Drive
Fort Lee, New Jersey 07027-1298

Dear Ms. Wrenn:

As you are aware, the Center for Veterinary Medicine was charged with examining previously approved antimicrobial products as a result of an amendment to the FY 2001 appropriations sponsored by U.S. Representative Sherrod Brown. As part of that effort, we have completed our review of the administrative file for your Aureo S-P250® (NADA 035-688); CSP™ 250 (NADA 039-077); and –Chlorachel™ 250 (NADA 091-668).

Our review included an examination of the correspondence contained in, data submitted to, and master files referenced in, the administrative file. We conducted a qualitative risk assessment in light of the Center's recently published Guidance for Industry #152 entitled, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," using the information contained in the records.

We are taking this opportunity to provide you with a summary of our findings:

Aureo S-P250® (NADA 035-688)

- The product is a Type A medicated article intended to produce a Type C medicated feed consisting of 100 grams of chlortetracycline, 50 grams of procaine penicillin, and 100 grams of sulfamethazine per ton of feed.

- The codified indication is: "for reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibrionic dysentery), prevention of these diseases during times of stress; maintenance of weight gains in the presence of atrophic rhinitis; growth promotion and increased feed efficiency in swine weighing up to 75 pounds.

- Protocols and data to address 21 CFR 135.109/558.15 were submitted. The requirements of 21 CFR 558.15 were not met.

- CVM's proposal to withdraw Aureo S-P250® remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

CSP™ 250 (NADA 039-077)

- The product is a Type A medicated article intended to produce a Type C medicated feed consisting of 100 grams of chlortetracycline, 50 grams of procaine penicillin, and 100 grams of sulfathiazole per ton of feed.

- The codified indication is: "for reduction of the incidence of cervical abscesses; treatment of bacterial enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibrionic dysentery), maintenance of weight gains in the presence of atrophic rhinitis; swine 10 lbs of body weight to 6 weeks post weaning: increased rate of weight gain and improved feed efficiency. Swine 6 to 16 weeks post weaning: increased rate of weight gain." (21 CFR 558.155).

- Protocols and data to address 21 CFR 135.109/558.15 were submitted. The requirements of 21 CFR 558.15 were not met.

- CVM's proposal to withdraw CSP™ 250 remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

Chlorachel™ 250 (NADA 091-668)

- The product is a Type A medicated article intended to produce a Type C medicated feed consisting of 100 grams of chlortetracycline, 50 grams of penicillin and 100 grams of sulfamethazine.

- The codified indication is: "It is administered to swine in a Type C feed for reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibrionic dysentery); prevention of these diseases during times of stress; maintenance of weight gains in the presence of atrophic rhinitis; growth promotion and increased feed efficiency in swine weighing up to 75 pounds." (21 CFR 558.145).

- Protocols and data to address 21 CFR 135.109/558.15 were submitted. The requirements of 21 CFR 558.15 were not met.

- CVM's proposal to withdraw Chlorachel™ 250 remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

The administrative record does not contain sufficient information to alleviate the Center's concern about the use of these products and their possible role in the emergence and dissemination of antimicrobial resistance. We used only that information on penicillin, tetracycline, sulfathiazole, and sulfamethazine contained in your administrative files to evaluate your products. Where information on your specific products was lacking, we generally took a

conservative approach and assessed the risk as high. The outcome of the qualitative risk assessment conducted according to Guidance #152 is that the product is considered Category 1. Production claims for weight gain, maintenance of weight gains in the presence of atrophic rhinitis and for growth promotion and increased feed efficiency in swine are not considered appropriate for Category 1 or 2 products under Guidance #152.

The Center for Veterinary Medicine would like to invite you to meet with us and discuss our findings. Please contact my office as soon as possible to arrange this. If you have any questions please contact Dr. Linda Tollefson, Deputy Director at 301-827-2950.

Sincerely yours,

Stephen F. Sundlof, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

cc: NADA 035-688
NADA 039-077
NADA 091-668
Director, Office of New Animal Drug Evaluation
Division Director, Human Food Safety

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 26 2004

Gregory P. Bergt
Director, Regulatory Affairs
Pennfield Oil Company
14040 Industrial Road
Omaha, NE 68144

Dear Mr. Bergt:

As you are aware, the Center for Veterinary Medicine was charged with examining previously approved antimicrobial products as a result of an amendment to the FY 2001 appropriations sponsored by U.S. Representative Sherrod Brown. As part of that effort, we have completed our review of the administrative file for your Pennchlor SP 250 and Pennchlor SP 500 (NADA 138-934).

Our review included an examination of the correspondence contained in, data submitted to, and master files referenced in, the administrative file. We conducted a qualitative risk assessment in light of the Center's recently published Guidance for Industry #152 entitled, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," using the information contained in the records.

We are taking this opportunity to provide you with a summary of our findings:

- Both products are Type A medicated articles intended to produce a Type C medicated feed consisting of 100 grams of chlortetracycline, 50 grams of penicillin and 100 grams of sulfamethazine.

- The codified indication is: "It is administered to swine in a Type C feed for reduction of the incidence of cervical abscesses; treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis* and vibrionic dysentery); prevention of these diseases during times of stress; maintenance of weight gains in the presence of atrophic rhinitis; growth promotion and increased feed efficiency in swine weighing up to 75 pounds." (21 CFR 558.145).

- Protocols and data to address 21 CFR 135.109/558.15 were submitted. The requirements of 21 CFR 558.15 were not met.

- CVM's proposal to withdraw penicillin premixes remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

The administrative record does not contain sufficient information to alleviate the Center's concern about the use of your product and its possible role in the emergence and dissemination of antimicrobial resistance. We used only that information on penicillin, tetracycline, and sulfamethazine contained in your administrative file to evaluate your product. Where information on your specific product was lacking, we generally took a conservative approach and assessed the risk as high. The outcome of the qualitative risk assessment conducted according to Guidance #152 is that the product is considered Category 1. Production claims for maintenance of weight gains in the presence of atrophic rhinitis and for growth promotion and increased feed efficiency are not considered appropriate for Category 1 or 2 products under Guidance #152.

The Center for Veterinary Medicine would like to invite you to meet with us and discuss our findings. Please contact my office as soon as possible to arrange this. If you have any questions please contact Dr. Linda Tollefson, Deputy Director at 301-827-2950.

Sincerely yours,

Stephen F. Sundlof, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

cc: NADA 138-934
Director, Office of New Animal Drug Evaluation
Division Director, Human Food Safety

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 26 2004

Norma A. Buckart
Manager, Regulatory Affairs
Phibro Animal Health
710 Rt. 46 East
Suite 401
Fairfield, NJ 07004

Dear Ms. Buckart:

As you are aware, the Center for Veterinary Medicine was charged with examining previously approved antimicrobial products as a result of an amendment to the FY 2001 appropriations sponsored by U.S. Representative Sherrod Brown. As part of that effort, we have completed our review of the administrative file for your Penicillin G Procaine 50% (Type A Medicated Article, NADA 46-668).

Our review included an examination of the correspondence contained in, data submitted to, and master files referenced in, the administrative file. We conducted a qualitative risk assessment in light of the Center's recently published Guidance for Industry #152 entitled, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," using the information contained in the records.

We are taking this opportunity to provide you with a summary of our findings:

- The codified indications are: "For increased rate of weight gain and improved feed efficiency."
- No data were found to address 21 CFR 558.15 or GFI #152.
- CVM's proposal to withdraw penicillin premixes remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

The administrative record does not contain sufficient information to alleviate the Center's concern about the use of your product and its possible role in the emergence and dissemination of antimicrobial resistance. We used only that information on penicillin contained in your administrative file to evaluate your product. Where information on your specific product was lacking, we generally took a conservative approach and assessed the risk as high. The outcome of the qualitative risk assessment conducted according to Guidance #152 is that the product is considered Category 1. Production claims for increased rate of weight gain and improved feed efficiency are not considered appropriate for Category 1 or 2 products under Guidance #152.

The Center for Veterinary Medicine would like to invite you to meet with us and discuss our findings. Please contact my office as soon as possible to arrange this. If you have any questions please contact Dr. Linda Tollefson, Deputy Director at 301-827-2950.

Sincerely yours,

Stephen F. Sundlof, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

cc: NADA 046-668
Director, Office of New Animal Drug Evaluation
Division Director, Human Food Safety

Citizen Petition Seeking Withdrawal of Approvals of Certain Herdwide/Flockwide Uses of Critically and Highly Important Antibiotics Pursuant to Guidance #152

Addendum: List of Approvals For Which Withdrawal is Sought

*** See below for footnotes**

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	0.1 mg/lb bw/day			128	(e)(4)(i)	Cattle	Revoke	Calves (up to 250 lb) increased rate of weight gain and improved feed efficiency	NS	In milk replacers or starter feed, include on labeling the warning ``A withdrawal period has not been established for this product in preruminating calves Do not use in calves to be processed for veal ''
Chlortetracycline	Tetracycline	25-70 mg/head/day			128	(e)(4)(vi)	Cattle	Revoke	Calves (250 to 400 lb) For increased rate of weight gain and improved feed efficiency	NS	In milk replacers or starter feed, include on labeling the warning ` A withdrawal period has not been established for this product in preruminating calves Do not use in calves to be processed for veal ''
Chlortetracycline	Tetracycline	70 mg/head/day			128	(e)(4)(vii)	Cattle	Revoke	Growing cattle (over 400 lb) For increased rate of weight gain, improved feed efficiency, and reduction of liver condemnation *due to liver abscesses*	NS	In milk replacers or starter feed, include on labeling the warning ` A withdrawal period has not been established for this product in preruminating calves Do not use in calves to be processed for veal ''
Chlortetracycline	Tetracycline	350 mg/head/day			128	(e)(4)(viii)(1)	Cattle	Revoke	1 Beef cattle For control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp susceptible to chlortetracycline	NS	Withdraw 48 h prior to slaughter For sponsor 046573 zero withdrawal time For sponsor 053389 1 d withdrawal time
Chlortetracycline	Tetracycline	350 mg/head/day	Sulfamethazine	350 mg/head/day	140	ALL	Cattle	Revoke	Aid in the maintenance of weight gains in the presence of respiratory disease such as shipping fever	28 days	Feed for 28 days, withdraw 7 days prior to slaughter
Chlortetracycline	Tetracycline	500-1000 g/ton	Decoquinate	13 6-27.2 g/ton	195	(e)(2)(?)***	Cattle	Amend	Calves, beef and nonlactating dairy cattle For the prevention of coccidiosis caused by Eimeria bovis and E zuernii, for treatment of bacterial enteritis caused by *Escherichia coli, for bacterial pneumonia caused by* Pasteurella multocida organisms susceptible to chlortetracycline	???	???
Chlortetracycline	Tetracycline	400 g/ton	Decoquinate	13.6-27 2 g/ton	195	(e)(2)(iii)	Cattle	Amend	Calves, beef and nonlactating dairy cattle For prevention of coccidiosis caused by Eimeria bovis and E zuernii, for treatment of bacterial enteritis caused by E. coli, and for treatment of bacterial pneumonia caused by Pasteurella multocida organisms susceptible to chlortetracycline	5-28 days	Feed Type C feed to provide 22 7 mg decoquinate and 1 gram (g) chlortetracycline per 100 lb body weight (0 5 mg/kg) per day for not more than 5 days Type C feed may be prepared from Type B feed containing 535 8 to 5,440 g/ton decoquinate and 6,700 to 80,000 g/ton chlortetracycline When consumed, feed 22 7 mg decoquinate per 100 lb body weight/day for a total of 28 days to prevent coccidiosis Withdraw 24 hours *prior to slaughter when manufactured from* CTC (chlortetracycline) Type A medicated articles under NADA 141-147 Zero withdrawal time when manufactured from AUREOMYCIN (chlortetracycline) Type A medicated articles under NADA 141-185 Do not feed to calves to be processed for veal Do not feed to animals producing milk for food
Tylosin	Macrolide	8-10 g/ton	Decoquinate, monensin	13.6-27 2, 5-30 g/ton	195	(e)(2)(v)	Cattle	Revoke	Cattle fed in confinement for slaughter For prevention *of coccidiosis caused by Eimeria bovis and E zuernii*, for improved feed efficiency, and for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	C	Feed only to cattle fed in confinement for slaughter Feed continuously as the sole ration to provide 22 7 mg of decoquinate per 100 lb body weight per day, 50 to 360 mg of monensin per head per day, and 60 to 90 mg of tylosin per head per day Feed at least 28 days during period of exposure to coccidiosis or when it is likely to be a hazard Do not feed to animals producing milk for food Also see paragraph (d)(1) of this section and Sec 558 355(d)(8) Monensin and tylosin as provided by No 000986 in Sec 510 600(c) of this *chapter*
Erythromycin	Macrolide	37 mg/head/day			248	(d)(2)	Cattle	Revoke	In feed for feedlot beef cattle at 37 milligrams per head per day as an aid in stimulating growth and improving feed efficiency	NS	
Chlortetracycline	Tetracycline	10 mg/lb bw	Laidlomycin	5 g/ton	305	(e)(2)	Cattle	Amend	For improved feed efficiency and increased rate of weight gain, treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida organisms susceptible to chlortetracycline	5 days	Feed continuously at a rate of 30 to 75 mg laidlomycin propionate potassium per head per day for not more than 5 days A withdrawal period has not been established for this product in pre-ruminating calves Do not use in calves to be processed for veal

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	350 mg/head/day	Laidlomycin	5 g/ton	305	(e)(3)	Cattle	Revoke	For improved feed efficiency and increased rate of weight gain, control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp susceptible to chlortetracycline	C	Feed continuously at a rate of 30 to 75 mg laidlomycin propionate potassium per head per day A withdrawal period has not been established for this product in pre-ruminating calves Do not use in calves to be processed for veal
Chlortetracycline	Tetracycline	10 mg/lb bw	Laidlomycin	5-10 g/ton	305	(e)(5)	Cattle	Amend	For improved feed efficiency, and for treatment of bacterial enteritis caused by E coli and bacterial pneumonia caused by P multocida organisms susceptible to chlortetracycline	5 days	Feed continuously at a rate of 30 to 150 mg laidlomycin propionate potassium per head per day for not more than 5 days A withdrawal period has not been established for this product in pre-ruminating calves Do not use in calves to be processed for veal
Chlortetracycline	Tetracycline	350 mg/head/day	Laidlomycin	5-10 g/ton	305	(e)(6)	Cattle	Revoke	For improved feed efficiency, and for control of bacterial pneumonia associated with shipping fever complex caused by Pasteurella spp susceptible to chlortetracycline	C	Feed continuously at a rate of 30 to 150 mg laidlomycin propionate potassium per head per day A withdrawal period has not been established for this product in pre-ruminating calves Do not use in calves to be processed for veal
Oxytetracycline	Tetracycline	7.5 g/ton	Lasalocid	10-30 g/ton	311	(e)(1)(vi)	Cattle	Revoke	Cattle for improved feed efficiency and reduction of incidence and severity of liver abscesses	C	In Type C feeds, for beef cattle fed in confinement for slaughter, feed continuously at 100 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline As monoalkyl (C8-C18) trimethyl ammonium oxytetracycline
Oxytetracycline	Tetracycline	7 5 g/ton	Lasalocid	25-30 g/ton	311	(e)(1)(vii)	Cattle	Revoke	Cattle for improved feed efficiency, increased rate of weight gain, and reduction of incidence and severity of liver abscesses	C	In Type C feeds, for beef cattle fed in confinement for slaughter, feed continuously at 250 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline As monoalkyl (C8-C18) trimethyl ammonium oxytetracycline
Oxytetracycline	Tetracycline	75 g/ton	Melengestrol	0 25-0.5 g/ton	342	(e)(1)(viii)	Cattle	Revoke	Heifers fed in confinement for slaughter For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat) For reduction of liver condemnation due to liver abscesses	NS	Add at the rate of 0 5 to 2 0 lb/head/day a medicated feed (liquid or dry) containing 0 125 to 1 0 mg melengestrol acetate/lb per pound to a feed containing 6 to 10 g oxytetracycline per ton; or add at the rate of 0 5 to 2 0 lb/head/day a dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate plus 37 5 to 150 mg oxytetracycline/lb to provide 0.25 to 0 5 mg melengestrol acetate and 75 mg oxytetracycline/head/day Oxytetracycline as provided by No 066104 in Sec 510 600(c) of this chapter
Tylosin	Macrolide	90 g/ton	Melengestrol, lasalocid	0.25-0.5, 100-360 g/ton	342	(e)(1)(iv)	Cattle	Revoke	Heifers fed in confinement for slaughter For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat) For reduced incidence of liver abscesses	NS	To administer 0 25 to 0 5 mg melengestrol acetate plus 100 to 360 mg lasalocid plus 90 mg tylosin/head/day 1 Add 0 5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate/lb to a medicated feed containing 10 to 30 g lasalocid and 8 to 10 g tylosin per ton, or 2 Add 0 5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate plus 50 to 720 mg lasalocid/lb to 4 5 to 18 lb of a dry medicated feed containing 10 to 40 g tylosin per ton, or 3 Add 0 5 to 2 0 lb/head/day of a dry pelleted medicated feed containing 0 125 to 1 0 mg melengestrol acetate (from a dry Type A article), 50 to 720 mg lasalocid, and 45 to 180 mg tylosin/lb to a ration of nonmedicated feed Lasalocid provided by No Alpharma and tylosin as tylosin phosphate by No 000986 in Sec 510 600(c) of this chapter

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Tylosin	Macrolide	60-90 g/ton	Melengestrol, monensin	0.25-0.5, 50-360 g/ton	342	(e)(1)(vii)	Cattle	Revoke	Heifers fed in confinement for slaughter For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat). For the prevention and control of coccidiosis due to E bovis and E zuernii, and for reduced incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	NS	To administer 0 25 to 0 5 mg melengestrol acetate plus 50 to 360 mg lasalocid plus 60 to 90 mg tylosin/head/day 1 Add 0 5 to 2 0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate/lb to a medicated feed containing 5 to 30 g monensin and 8 to 10 g tylosin per ton, or 2 Add 0 5 to 2 0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate plus 25 to 720 mg monensin/lb to 4 5 to 18 lb of a dry medicated feed containing 10 to 40 g tylosin per ton; or 3 Add 0 5 to 2 0 lb/head/day of a dry pelleted medicated feed containing 0 125 to 1 0 mg melengestrol acetate (from a dry Type A article), 25 to 600 mg monensin, and 45 to 180 mg tylosin/lb to a ration of nonmedicated feed Monensin and tylosin as tylosin phosphate by No 000986 in Sec 510 600(c) of this chapter
Tylosin	Macrolide	60-90 g/ton	Melengestrol	0 25-0.5 g/ton	342	(e)(1)(ix)	Cattle	Revoke	Heifers fed in confinement for slaughter For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat) For reduced incidence of liver abscesses caused by F necrophorum and Actinomyces (Corynebacterium) pyogenes	NS	To administer 0 25 to 0 5 mg melengestrol acetate with 60 to 90 mg tylosin/head/day 1 Add 0 5 to 2 0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate/lb to a medicated feed containing 8 to 10 g tylosin per ton, or 2 Add 0 5 to 2 0 lb/head/day of a liquid or dry medicated feed containing 0 125 to 1 0 mg melengestrol acetate/lb to 4 5 to 18 lb of a dry medicated feed containing 10 to 40 g tylosin per ton, or 3 Add 0 5 to 2 0 lb/head/day of a dry pelleted medicated feed containing 0 125 to 1 0 mg melengestrol acetate (from a dry Type A article) plus 45 to 180 mg tylosin/lb to a ration of nonmedicated feed Tylosin as tylosin phosphate by No 000986 in Sec 510 600(c) of this chapter.
Tylosin	Macrolide	8-10 g/ton	Monensin	5-30 g/ton	355	(f)(3)(ii)	Cattle	Revoke	Improved feed efficiency, for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) *pyogenes*	C	Feed only to cattle being fed in confinement for slaughter Feed continuously as sole ration at the rate of 50 to 360 milligrams of monensin and 60 to 90 milligrams of tylosin per head per day, as monensin sodium, as tylosin phosphate Combination drug liquid *Type B medicated feeds may be used to manufacture* dry Type C medicated feeds and shall conform to mixing instructions as in Sec 558 625 (c)
Tylosin	Macrolide	150 g/ton	Monensin	400 g/ton	355	(f)(3)(ix)	Cattle	Revoke	*Improved feed efficiency, for reduction of incidence of* liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	C	Feed only to cattle being fed in confinement for slaughter Feed continuously at the rate of 8 2 to 10 2 kilograms (18 to 22 5 pounds) of Type C medicated feed per head per day to supply 240 milligrams of monensin and 90 milligrams of tylosin per head per day, as monensin sodium, as tylosin phosphate Do not allow horses or other equines access to feeds containing monensin Ingestion of monensin by equines has been fatal Safe use in unapproved species and breeding cattle has not been established The liquid Type B medicated feed must bear an expiration date of 14 days after date of manufacture The mixing directions for this liquid Type B medicated feed stored in recirculation or agitation tank systems are Recirculate or agitate immediately prior to use for not less than 10 minutes, moving at least 1 percent of the tanks contents per minute from the bottom of the tank to the top. Recirculate or agitate as directed daily, even when the Type B medicated feed is not used Inadequate mixing (recirculation or agitation) of liquid Type B medicated feeds may result in increased moner

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Tylosin	Macrolide	8-10 g/ton	Monensin	10-30 g/ton	355	(f)(3)(xii)	Cattle	Revoke	For improved feed efficiency, prevention and control of coccidiosis due to Eimena bovis and E zuernii, and reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	C	Feed only to cattle being fed in confinement for slaughter Feed continuously to provide 50 to 360 milligrams monensin per head per day For prevention and control of coccidiosis, feed at a rate of 0 14 to 0.42 milligram monensin per pound of body weight per day, depending upon the severity of challenge, up to maximum of 360 milligrams per head per day, and 60 to 90 milligram of tylosin per head per day
Oxytetracycline	Tetracycline	0.05 to 0 1 mg/lb bw/day			450	(d)(1)(viii)	Cattle	Revoke	Calves (up to 250 lb), for increased rate of weight gain and improved feed efficiency	C	Feed continuously, in milk replacers or starter feed
Oxytetracycline	Tetracycline	25 mg/head/day			450	(d)(1)(xi)	Cattle	Revoke	Calves (250 to 400 lb), increased rate of weight gain and improved feed efficiency	NS	
Oxytetracycline	Tetracycline	75 mg/head/day			450	(d)(1)(xii)	Cattle	Revoke	Growing cattle (over 400 lb), increased rate of weight gain, improved feed efficiency, and reduction of liver condemnation due to liver abscesses	NS	
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin	8 2-24 6, 10-30 g/ton	500	(e)(2)(iv)	Cattle	Revoke	Cattle fed in confinement for slaughter For increased rate of weight gain and improved feed efficiency during the last 28 to 42 days on feed, for prevention and control of coccidiosis due to E bovis and E zuernii, and for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed Not for animals intended for breeding
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin, melengesterol acetate	9.8-24.6, 10-30 g/ton, 0.25-0.5 mg/head/day	500	(e)(2)(?)***	Cattle	Revoke	For prevention and control of coccidiosis due to Eimena bovis and E zuernii; for reduction of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes, improved feed efficiency, increased rate of weight gain, for increased carcass leanness, and for suppression of estrus (heat)	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed Not for animals intended for breeding
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin	9 8-24 6, 10-30 g/ton	500	(e)(2)(ix)	Cattle	Revoke	Cattle fed in confinement for slaughter For increased rate of weight gain and improved feed efficiency during the last 28 to 42 days on feed; for prevention and control of coccidiosis due to E bovis and E zuernii, and for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed Not for animals intended for breeding
Tylosin	Macrolide	8-10 g/ton			625	(f)(1)(i)	Cattle	Revoke	For reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes	C	As tylosin phosphate, each animal must receive not more than 90 milligrams per day and not less than 60 milligrams per day, feed continuously as sole ration
Virginiamycin	Streptogramin	16-22 5 g/ton			635	(d)(3)(i)	Cattle	Revoke	For increased rate of weight gain	C	Feed continuously as sole ration to cattle fed in confinement for slaughter Not for use in animals intended for breeding
Virginiamycin	Streptogramin	13 5-16 g/ton			635	(d)(3)(ii)	Cattle	Revoke	For reduction of incidence of liver abscesses	C	Feed continuously as sole ration to cattle fed in confinement for slaughter Not for use in animals intended for breeding
Virginiamycin	Streptogramin	11-16 g/ton			635	(d)(3)(iii)	Cattle	Revoke	For improved feed efficiency	C	Feed continuously as sole ration to cattle fed in confinement for slaughter Not for use in animals intended for breeding
Sulfanitran	Sulfonamide	181.6 g/ton	Aklomide	227 g/ton	35	(c)(2)	Poultry	Revoke	Chickens As an aid in the prevention of coccidiosis caused by E tenella, E necatrix, and E acervulina	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter
Sulfanitran	Sulfonamide	181.6 g/ton	Aklomide, roxarsone	227, 22.7-45.4 g/ton	35	(c)(3)	Poultry	Revoke	Chickens As an aid in the prevention of coccidiosis caused by E tenella, E necatrix, and E acervulina, growth promition and feed efficiency, improving pigmentation	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter, as sole source of organic arsenic, chickens should have access to drinking water at all times
Chlortetracycline	Tetracycline	100-200 g/ton	Amprolium	36 3-113 5 g/ton	55	(d)(2)(i)	Poultry	Amend	Chickens, development of active immunity to coccidiosis, control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d
Chlortetracycline	Tetracycline	200-400 g/ton	Amprolium	36 3-113.5 g/ton	55	(d)(2)(i)	Poultry	Amend	Chickens, development of active immunity to coccidiosis, control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and E coli susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	100-200 g/ton	Amprolium	72 6-113 5 g/ton	55	(d)(2)(ii)	Poultry	Amend	Chickens, prevention of coccidiosis caused by E tenella only, control of infectious synovitis caused by M synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d
Chlortetracycline	Tetracycline	200-400 g/ton	Amprolium	72.6-113 5 g/ton	55	(d)(2)(ii)	Poultry	Amend	Chickens, prevention of coccidiosis caused by E tenella only, control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and E coli susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d
Chlortetracycline	Tetracycline	100-200 g/ton	Amprolium	113 5-227, 90 g/ton	55	(d)(2)(iv)	Poultry	Amend	Chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, control of infectious synovitis caused by M synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d
Erythromycin	Macrolide	4 6-18 5 g/ton	Amprolium, arsanilic acid	36 3-113 5, 90 g/ton	55	(d)(2)(i)	Poultry	Revoke	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency, improving pigmentation	NS	Withdraw 5 d before slaughter
Erythromycin	Macrolide	92.5 g/ton	Amprolium, arsanilic acid	36.3-113 5, 90 g/ton	55	(d)(2)(i)(1)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency, improving pigmentation, as an aid in the prevention of chronic respiratory disease during periods of stress	5-8 days	Feed for 2 d before stress and 3 to 6 d after stress, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	92 5 g/ton	Amprolium, arsanilic acid	36 3-113 5, 90 g/ton	55	(d)(2)(i)(2)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency, improving pigmentation, as an aid in the prevention of infectious coryza	7-14 days	Feed for 7 to 14 d, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	185 g/ton	Amprolium, arsanilic acid	36 3-113 5, 90 g/ton	55	(d)(2)(i)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency; improving pigmentation, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	4.6-18 5 g/ton	Amprolium	36.3-113.5 g/ton	55	(d)(2)(i)	Poultry	Revoke	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency	NS	As erythromycin thiocyanate
Erythromycin	Macrolide	92.5 g/ton	Amprolium	36 3-113.5 g/ton	55	(d)(2)(i)	Poultry	Amend	1 Replacement chickens, development of active immunity to coccidiosis, as an aid in the prevention of infectious coryza 2 Replacement chickens, development of active immunity to coccidiosis, as an aid in the prevention of chronic respiratory disease during periods of stress	5-14 days	1 Feed for 7 to 14 d, withdraw 24 h before slaughter Feed according to subtable in item (i) 2 Feed for 2 d before stress and 3 to 6 d after stress, withdraw 24 h before slaughter Feed according to subtable in item (i)
Erythromycin	Macrolide	185 g/ton	Amprolium	36 3-113 5 g/ton	55	(d)(2)(i)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, as an aid in the prevention and reduction of lesions and in lowering seventy of chronic respiratory disease	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 48 h before slaughter Feed according to subtable in item (i)
Erythromycin	Macrolide	4.6-18 5 g/ton	Amprolium, arsanilic acid	113.5-227, 90 g/ton	55	(d)(2)(iv)	Poultry	Revoke	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency, improved pigmentation	NS	Withdraw 5 d before slaughter
Erythromycin	Macrolide	92.5 g/ton	Amprolium, arsanilic acid	113 5-227, 90 g/ton	55	(d)(2)(iv)(1)	Poultry	Amend	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency, improving pigmentation, as aid in the prevention of chronic respiratory disease during periods of stress	5-8 days	Feed for 2 d before stress and 3 to 6 d after stress, withdraw 5 d before slaughter; as sole source of organic arsenic
Erythromycin	Macrolide	92.5 g/ton	Amprolium, arsanilic acid	113 5-227, 90 g/ton	55	(d)(2)(iv)(2)	Poultry	Amend	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency, improving pigmentation, as an aid in the prevention of infectious coryza	7-14 days	Feed for 7 to 14 d, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	185 g/ton	Amprolium, arsanilic acid	113 5 227, 90 g/ton	55	(d)(2)(iv)	Poultry	Amend	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis; growth promotion and feed efficiency, improving pigmentation, as an aid in the prevention and reduction of lesions and in lowering seventy of chronic respiratory disease	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	4.6-18.5 g/ton	Amprolium	113.5-227 g/ton	55	(d)(2)(iv)	Poultry	Revoke	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency	NS	As erythromycin thiocyanate

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Erythromycin	Macrolide	92 5 g/ton	Amprolium	113 5-227 g/ton	55	(d)(2)(iv)	Poultry	Amend	1 Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention of chronic respiratory disease during periods of stress 2 Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis, as an aid in the prevention of infectious coryza	5-14 days	1 Feed for 2 d before stress and 3 to 6 d after stress, withdraw 24 h before slaughter. 2 Feed for 7 to 14 d, withdraw 24 h before slaughter
Erythromycin	Macrolide	185 g/ton	Amprolium	113 5-227 g/ton	55	(d)(2)(iv)	Poultry	Amend	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 48 h before slaughter
Penicillin procaine	Penicillin	2.4-50 g/ton	Amprolium	36.3-113.5 g/ton	55	(d)(2)(i)	Poultry	Revoke	Replacement chickens, development of active immunity to coccidiosis, growth promotion and feed efficiency	NS	As procaine penicillin
Penicillin procaine	Penicillin	2.4-50 g/ton	Amprolium	72 6-113.5 g/ton	55	(d)(2)(ii)	Poultry	Revoke	Broiler chickens, prevention of coccidiosis caused by E tenella only, growth promotion and feed efficiency	NS	As procaine penicillin
Penicillin procaine	Penicillin	2.4-50 g/ton	Amprolium	113.5-227 g/ton	55	(d)(2)(iv)	Poultry	Revoke	1 Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis, growth promotion and feed efficiency	NS	As procaine penicillin
Chlortetracycline	Tetracycline	100-200 g/ton	Amprolium, ethopabate	113 5-227, 3.6 g/ton	58	(d)(1)(iv)	Poultry	Amend	For chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption Feed for 7 to 14 d
Chlortetracycline	Tetracycline	200-400 g/ton	Amprolium, ethopabate	113.5-227, 3.6 g/ton	58	(d)(1)(iv)	Poultry	Amend	For chickens where immunity to coccidiosis is not desired, prevention of coccidiosis; control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and E coli susceptible to chlortetracycline	7-14 days	In low calcium feed containing 0 8% dietary calcium and 1.5% sodium sulfate, feed continuously as sole ration for 7 to 14 d, do not feed to chickens producing eggs for human consumption
Erythromycin	Macrolide	4.6-18 5 g/ton	Amprolium, ethopabate, arsanilic acid	113.5, 36.3 g/ton	58	(d)(1)(iii)	Poultry	Revoke	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency; improve pigmentation	NS	Not for laying hens, withdraw 5 d before slaughter, as sole source of organic arsenic, as erythromycin thiocyanate
Erythromycin	Macrolide	4 6-18.5 g/ton	Amprolium, ethopabate	113 5, 36 3 g/ton	58	(d)(1)(iii)	Poultry	Revoke	Broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis, growth promotion and feed efficiency	NS	Not for laying hens, withdraw 24 hours before slaughter, erythromycin thiocyanate
Erythromycin	Macrolide	92.5 g/ton	Amprolium, ethopabate, arsanilic acid	113.5-227, 3.6 g/ton	58	(d)(1)(iv)(1)	Poultry	Amend	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention of chronic respiratory disease during periods of stress, growth promotion and feed efficiency, improving pigmentation	5-8 days	Feed for 2 d before stress and 3 to 6 d after stress, withdraw 5 d before slaughter, as sole source of organic arsenic, not for laying hens
Erythromycin	Macrolide	92 5 g/ton	Amprolium, ethopabate, arsanilic acid	113.5-227, 3.6 g/ton	58	(d)(1)(iv)(2)	Poultry	Amend	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention of infectious coryza, growth promotion and feed efficiency, improving pigmentation	7-14 days	Feed for 7 to 14 d, withdraw 5 d before slaughter, as sole source of organic arsenic, not for laying hens
Erythromycin	Macrolide	185 g/ton	Amprolium, ethopabate	113 5-227, 3 6 g/ton	58	(d)(1)(iv)	Poultry	Amend	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, growth promotion and feed efficiency; improving pigmentation	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	92 5 g/ton	Amprolium, ethopabate	113.5-227, 3.6 g/ton	58	(d)(1)(iv)	Poultry	Amend	1 For broiler chickens and for replacement chickens where immunity to coccidiosis is not desired: prevention of coccidiosis, as an aid in the prevention of chronic respiratory disease during periods of stress 2 For broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, as an aid in the prevention of infectious coryza	5-14 days	1 Feed for 2 d before stress and 3 to 6 d after stress, withdraw 24 h before slaughter, not for laying hens 2 Feed for 7 to 14 d, withdraw 24 h before slaughter, not for laying hens

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Erythromycin	Macrolide	185 g/ton	Amprolium, ethopabate	113 5-227, 3 6 g/ton	58	(d)(1)(iv)	Poultry	Amend	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired; prevention of coccidiosis, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 48 h before slaughter
Lincomycin	Lincosamide	2-4 g/ton	Amprolium, ethopabate	113.5, 3 6 g/ton	58	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, for increase in rate of weight gain, *improved feed efficiency, as an aid in the prevention of* coccidiosis	NS	Not for laying chickens, as lincomycin hydrochloride monohydrate; as sole source of amprolium
Lincomycin	Lincosamide	2-4 g/ton	Amprolium, ethopabate, roxarsone	113.5, 3.6, 45.4 g/ton	58	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, for increase in rate of weight gain, improved feed efficiency and pigmentation, as an aid in the prevention of coccidiosis	NS	Not for laying chickens; as lincomycin hydrochloride monohydrate, withdraw 5 d before slaughter, as sole source of amprolium and organic arsenic
Penicillin procaine	Penicillin	2 4-50 g/ton	Amprolium, ethopabate	113 5-227, 3.6 g/ton	58	(d)(1)(iv)	Poultry	Revoke	For broiler chickens and replacement chickens where immunity to coccidiosis is not desired, prevention of coccidiosis, growth promotion and feed efficiency, improving pigmentation	NS	Not for laying hens, as procaine penicillin
Virginiamycin	Streptogramin	15 g/ton	Amprolium, ethopabate	113 5, 36 3 g/ton	58	(d)(1)(iii)	Poultry	Revoke	Broiler chickens, as an aid in the prevention of coccidiosis where severe exposure to Eimeria acervulina, E brunetti, and E maxima is likely to *occur, for increased rate of weight gain and improved* feed efficiency	C	Feed continuously as sole ration, do not feed to laying hens, not for chickens over 16 weeks of age, as sole source of amprolium, amprolium and ethopabate as *provided by Menal in Sec 510 600(c), virginiamycin as* provided by 066104
Virginiamycin	Streptogramin	5-15 g/ton g/ton	Amprolium, ethopabate	113 5, 36.3 g/ton	58	(d)(1)(iii)	Poultry	Revoke	Broiler chickens, as an aid in the prevention of coccidiosis where severe exposure to Eimeria acervulina, E brunetti, and E maxima is likely to occur, for increased rate of weight gain	C	Feed continuously as sole ration, do not feed to laying hens, not for chickens over 16 weeks of age, as sole source of amprolium, amprolium and ethopabate as provided by Menal in Sec. 510 600(c), virginiamycin as provided by 066104
Erythromycin	Macrolide	4 6 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(iii)	Poultry	Revoke	Chickens; growth promotion and feed efficiency, improving pigmentation	NS	As erythromycin thiocyanate, withdraw 5 days before slaughter; as sole source of organic arsenic
Erythromycin	Macrolide	4.6-18.5 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(iv)	Poultry	Revoke	Chickens; growth promotion and feed efficiency, improving pigmentation	NS	As erythromycin thiocyanate, withdraw 5 days before slaughter; as sole source of organic arsenic
Erythromycin	Macrolide	9.25 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(v)	Poultry	Revoke	Chickens; growth promotion and feed efficiency, improving pigmentation	NS	As erythromycin thiocyanate, withdraw 5 days before slaughter; as sole source of organic arsenic
Erythromycin	Macrolide	92 5 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(vi)(1)	Poultry	Amend	Chickens, as an aid in the prevention of chronic respiratory disease during periods of stress growth promotion and feed efficiency, improving pigmentation	5-8 days	As erythromycin thiocyanate, feed for 2 days before stress and 3 to 6 days after stress, withdraw 5 days before slaughter, as sole source of arsenic
Erythromycin	Macrolide	92.5 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(vi)(2)	Poultry	Amend	Chickens, as an aid in the prevention of infectious coryza, growth promotion and feed efficiency, improving pigmentation	7-14 days	As erythromycin thiocyanate, feed for 7 to 14 days, withdraw 5 days before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	185 g/ton	Arsanilic acid	90 g/ton	62	(c)(1)(vii)	Poultry	Amend	Chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, growth promotion and feed efficiency, improving pigmentation	5-8 days	As erythromycin thiocyanate, feed for 5 to 8 days, do not use in birds producing eggs for food purposes, withdraw 5 days before slaughter, as sole source of organic arsenic.
Chlortetracycline	Tetracycline	10-50 g/ton			128	(e)(1)(i)	Poultry	Revoke	Chickens For increased rate of weight gain and improved feed efficiency	NS	Do not feed to chickens producing eggs for human consumption
Chlortetracycline	Tetracycline	100-200 g/ton	Clopidol	113 5 g/ton	175	(d)(5)	Poultry	Amend	Broiler and replacement chickens As an aid in the prevention of coccidiosis caused by E tenella, E necatrix, E. acervulina, E maxima, E brunetti, and E mivati, for increased rate of weight gain and improved feed efficiency, for control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	7-14 days	Feed continuously as sole ration from the time chicks are placed in floor pens for 7 to 14 days
Lincomycin	Lincosamide	2-4 g/ton	Clopidol	113.5 g/ton	175	(d)(6)	Poultry	Revoke	Broiler chickens As an aid in the prevention of coccidiosis caused by E tenella, E necatrix, E *acervulina, E maxima, E brunetti, and E mivati, for* increased rate of weight gain and improved feed efficiency	NS	Do not feed to chickens over 16 weeks of age, as lincomycin hydrochloride monohydrate
Chlortetracycline	Tetracycline	100-200 g/ton	Decoquinate	27 2 g/ton	195	(e)(1)(vi)	Poultry	Amend	Broiler chickens For prevention of coccidiosis caused by Eimeria tenella, E necatrix, E mivati, E acervulina, E maxima, and E brunetti, control of infectious synovitis caused by Mycoplasma synoviae susceptible *to chlortetracycline*	7-14 days	Feed continuously for 7 to 14 days, do not feed to chickens producing eggs for human consumption

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	200-400 g/ton	Decoquinate	27 2 g/ton	195	(e)(1)(vii)	Poultry	Amend	Broiler chickens For prevention of coccidiosis caused by Eimena tenella, E necatrix, E mivati, E. acervulina, E. maxima, and E brunetti, and for control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and Escherichia coli susceptible to chlortetracycline	7-14 days	Feed continuously for 7 to 14 days, do not feed to chickens producing eggs for human consumption
Lincomycin	Lincosamide	2 g/ton	Decoquinate	27 2 g/ton	195	(e)(1)(viii)	Poultry	Revoke	Broiler chickens For prevention of coccidiosis caused by Eimena tenella, E necatrix, E mivati, E acervulina, E maxima, and E brunetti, and for increased rate of weight gain and improved feed efficiency	NS	Feed as sole ration, do not feed to laying chickens, lincomycin provided by No 000009 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5 g/ton	Diclazuril	0 91 g/ton	198	(d)(1)(vii)	Poultry	Revoke	Broiler chickens· For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E. brunetti, E mitis (mivati), and E maxima Because diclazuril is effective against E maxima later in its life cycle, subclinical intestinal lesions may be present or a short time after infection Diclazuril was shown in studies to reduce lesion scores and improve performance and health of birds challenged with E maxima; for increased rate of weight gain and improved feed efficiency	C	Feed continuously Not for use in hens producing eggs for human food, Virginiamycin provided by 066104
Virginiamycin	Streptogramin	5-15 g/ton	Diclazuril	0 91 g/ton	198	(d)(1)(viii)	Poultry	Revoke	Broiler chickens. For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E brunetti, E mitis (mivati), and E maxima Because diclazuril is effective against E maxima later in its life cycle, subclinical intestinal lesions may be present or a short time after infection Diclazuril was shown in studies to reduce lesion scores and improve performance and health of birds challenged with E maxima, for increased rate of weight gain	C	Feed continuously Not for use in hens producing eggs for human food, Virginiamycin provided by 066104
Erythromycin	Macrolide	4 6-18.5 g/ton			248	(d)(1)(i)	Poultry	Revoke	Chickens, growth promotion and feed efficiency	NS	
Erythromycin	Macrolide	92 5 g/ton			248	(d)(1)(v)	Poultry	Amend	1 Chickens, as an aid in the prevention of chronic respiratory disease during periods of stress 2 Chickens, as an aid in the prevention of infectious coryza	5-14 days	1 Feed for 2 d before stress and 3 to 6 d after stress, withdraw 24 h before slaughter 2 Feed for 7 to 14 d, withdraw 24 h before slaughter
Lincomycin	Lincosamide	2-4 g/ton	Halofuginone	2.72 g/ton	265	(c)(1)(vii)	Poultry	Revoke	Broiler chickens For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E brunetti, E mivati, and E maxima and for improved feed efficiency	C	Feed continuously as sole ration, withdraw 4 days before slaughter, do not feed to layers, avoid contact with skin, eyes, or clothing, keep out of lakes, ponds, or streams.
Virginiamycin	Streptogramin	5 g/ton	Halofuginone	2 72 g/ton	265	(c)(1)(iii)	Poultry	Revoke	Broiler chickens. For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E brunetti, E mivati, and E maxima, for increased rate of weight gain and improved feed efficiency	C	Feed continuously as sole ration, withdraw 6 days before slaughter, do not feed to layers
Virginiamycin	Streptogramin	5-15 g/ton	Halofuginone	2 72 g/ton	265	(c)(1)(iv)	Poultry	Revoke	Broiler chickens· For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E brunetti, E mevati, and E maxima, for increased rate of weight gain	C	Feed continuously as sole ration, withdraw 6 days before slaughter, do not feed to layers
Chlortetracycline	Tetracycline	100-200 g/ton	Hygromycin B	8-12 g/ton	274	(c)(1)(i)	Poultry	Amend	Chickens; control of infestation of large roundworms (Ascaris galli), cecal worms (Heterakis gallinae), and capillary worms (Capillana obsignata), control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption; feed for 7 to 14 days; withdraw 3 days before slaughter.
Chlortetracycline	Tetracycline	200-400 g/ton	Hygromycin B	8-12 g/ton	274	(c)(1)(i)	Poultry	Amend	Chickens; control of infestation of large roundworms (Ascaris galli), cecal worms (H Gallinae), and capillary worms (Capillana obsignata), control of chronic respiratory disease (CRD) and air sac infection caused by Mycoplasma gallisepticum and Escherichia coli susceptible to chlortetracycline.	7-14 days	Do not feed to chickens producing eggs for human consumption, feed for 7 to 14 days, withdraw 3 days before slaughter

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Penicillin procaine	Penicillin	100-200 g/ton	Hygromycin B, bacitracin	8-12 g/ton, combo	274	(c)(1)(i)	Poultry	Amend	1 Chickens, control of infestation of large roundworms (Ascaris galli), cecal worms (Heterakis gallinae), and capillary worms (Capillaria obsignata), treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis) 2 Chickens, control of infestation of large roundworms (Ascaris galli), cecal worms (Heterakis gallinae), and capillary worms (Capillaria obsignata), treatment of chronic respiratory disease (airsac infection), blue comb (nonspecific infectious enteritis)	NS	1 Feed containing not less than 25% of penicillin plus not less than 50% of bacitracin, as procaine penicillin plus bacitracin methylene disalicylate, withdraw 3 days before slaughter 2 Combination containing not less than 50% nor more than 75% of bacitracin, except that it contains not more than 125 g of penicillin, as procaine penicillin plus zinc bacitracin, withdraw 3 days before slaughter
Penicillin procaine	Penicillin	100 g/ton	Hygromycin B	8-12 g/ton	274	(c)(1)(i)	Poultry	Amend	Chickens, control of infestation of large roundworms (Ascaris galli), cecal worms (Heterakis gallinae), and capillary worms (Capillaria obsignata), treatment of chronic respiratory disease (airsac infection), blue *comb (nonspecific infectious enteritis)*	NS	As procaine penicillin Withdraw 3 days before slaughter
Tylosin	Macrolide	4-50 g/ton	Hygromycin B	8-12 g/ton	274	(c)(1)(i)	Poultry	Amend	Chickens Control of infestations of large roundworms (Ascaris galli), cecal worms (Heterakis gallinae,), and capillary worms (Capillaria obsignata), growth promotion and feed efficiency	NS	As tylosin phosphate, withdraw 3 days before slaughter
Lincomycin	Lincosamide	2 g/ton	Lasalocid, roxarsone	68-113, 45 4 g/ton	311	(e)(1)(ii)	Poultry	Revoke	Broiler chickens. For prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E brunetti, E mivati, and E maxima, as an aid in the reduction of lesions due to E tenella, and for increased rate of weight gain and improved feed efficiency	C	For broiler chickens only, feed continuously as sole ration, withdraw 5 days before slaughter, roxarsone provided by Nos Alpharma and 011526 in Sec 510 600(c) of this chapter, lincomycin provided by No 000009
Lincomycin	Lincosamide	2 g/ton	Lasalocid	68 g/ton	311	(e)(1)(iii)	Poultry	Revoke	Broiler or fryer chickens, for the prevention of coccidiosis caused by Eimena mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix, for increased rate of weight gain and improved feed efficiency	C	For broiler and fryer chickens only, feed continuously as sole ration, withdraw 5 d before slaughter, Type C feed must be used within 4 weeks of manufacture, as lincomycin hydrochloride monohydrate
Virginiamycin	Streptogramin	20 g/ton	Lasalocid	68 g/ton	311	(e)(1)(v)	Poultry	Revoke	For broiler and fryer chickens only For prevention of coccidiosis caused by Eimena tenella E necatrix, E acervulina, E brunetti, E mivati, and E maxima, and for increased rate of weight gain and improved feed efficiency	C	*For broiler and fryer chickens only, feed continuously* as sole ration, do not feed to laying chickens, lasalocid sodium provided by No Alpharma in 510 600(c) of this chapter
Lincomycin	Lincosamide	2 g/ton			325	(d)(1)(i)	Poultry	Amend	Broilers For control of necrotic enteritis caused by Clostridium spp or other susceptible organisms	NS	As lincomycin hydrochloride monohydrate
Lincomycin	Lincosamide	2-4 g/ton			325	(d)(1)(ii)	Poultry	Revoke	Broilers For increased rate of weight gain and improved feed efficiency	NS	As lincomycin hydrochloride monohydrate
Lincomycin	Lincosamide	2 g/ton	Monensin	90-110 g/ton	355	(f)(1)(ix)	Poultry	Revoke	Broiler chickens For increase in rate of weight gain and improved feed efficiency, as an aid in the prevention of coccidiosis caused by E necatrix, E tenella, E acervulina, E brunetti, E mivati, and E maxima	NS	Do not feed to laying chickens, to be fed as a sole ration, in the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain, as monensin sodium
Lincomycin	Lincosamide	2 g/ton	Monensin, roxarsone	90-110, 15-45 g/ton	355	(f)(1)(x)	Poultry	Revoke	Broiler chickens For increase in rate of weight gain, as an aid in the prevention of coccidiosis caused by E necatrix, E tenella, E acervulina, E brunetti, E mivati, and E maxima	C	Do not feed to laying chickens, feed continuously as the sole ration, withdraw 5 days before slaughter, as sole source of organic arsenic, as roxarsone provided *by No Alpharma, Sec 510 600(c) of this chapter, as* monensin sodium provided by No 000986, Sec 510 600(c) of this chapter, as lincomycin provided by No. 000009, Sec 510 600(c) of this chapter, as a combination provided by No. 000009, Sec 510 600(c) of this chapter
Lincomycin	Lincosamide	2 g/ton	Monensin, roxarsone	90-110, 15-30 g/ton	355	(f)(1)(xi)	Poultry	Revoke	Broiler chickens For increase in rate of weight gain, improved feed efficiency, improved pigmentation, and as an aid in the prevention of coccidiosis caused by E necatrix, E tenella, E acervulina, E brunetti, E mivati and E maxima	C	Do not feed to laying chickens, feed continuously as the sole ration, withdraw 5 days before slaughter, as sole source of organic arsenic, as roxarsone provided by No Alpharma in Sec 510 600(c) of this chapter, as monensin sodium provided by No 000986 in Sec. 510 600(c) of this chapter, as lincomycin provided by No 000009 in Sec 510 600(c) of this chapter, as a combination provided by No 000009 in Sec 510 600(c) of this chapter

Drug	Class	Dose	Combination drug(s)	Dose	21CFR§ subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Oxytetracycline	Tetracycline	200 g/ton	Monensin	90-110 g/ton	355	(f)(1)(viii)	Poultry	Amend	Broiler chickens As an aid in the prevention of coccidiosis caused by Eimeria necatrix, E tenella, E acervulina, E brunetti, E mivati, and E maxima, and for the control of complicated chronic respiratory disease (CRD or air-sac infection) caused by Mycoplasma gallisepticum and Escherichia coli	C	In the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain, do not feed to laying chickens, feed continuously as sole ration, as monensin sodium
Oxytetracycline	Tetracycline	500 g/ton	Monensin	90-110 g/ton	355	(f)(1)(xxii)	Poultry	Amend	Broiler chickens As an aid in the prevention of coccidiosis caused by Eimeria necatrix, E tenella, E acervulina, E brunetti, E Mivati, and E maxima, as an aid in the reduction of mortality due to air-sacculities (air-sac infection) caused by Escherichia coli sensitive to oxytetracycline	5 days	Feed for 5 days as sole ration Do not feed to laying chickens Withdraw 24 hours before slaughter As monensin sodium provided by No 000986 in Sec 510 600(c) of this chapter As mono-alkyl (C8-C18) trimethylammonium oxytetracycline provided by No 066104 in Sec 510 600(c) of this chapter
Tylosin	Macrolide	4-50 g/ton	Monensin	90-110 g/ton	355	(f)(1)(xxviii)	Poultry	Revoke	Broiler chickens As an aid in the prevention of coccidiosis caused by Eimeria necatrix, E tenella, E acervulina, E brunetti, E mivati, and E maxima, for increased rate of weight gain, and improved feed efficiency	C	Feed continuously as sole ration In the absence of coccidiosis, the use of monensin with no withdrawal period may limit feed intake resulting in reduced weight gain Do not feed to laying chickens As monensin sodium and tylosin phosphate provided by No 000986 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5 g/ton	Monensin	90-110 g/ton	355	(f)(1)(xiii)	Poultry	Revoke	Broiler chickens: As an aid in the prevention of coccidiosis caused by E necatrix, E tenella, E acervulina, E brunetti, E maxima, and E mivati, for increased rate of weight gain and improved feed efficiency	C	Do not feed to laying chickens, feed continuously as sole ration, as monensin sodium provided by No 000986 in Sec 510 600 of this chapter; virginiamycin provided by No 066104 in Sec. 510 600 of this chapter
Virginiamycin	Streptogramin	5-15 g/ton	Monensin, roxarsone	90-110, 22 7 g/ton	355	(f)(1)(xx)	Poultry	Revoke	Broiler chickens: For increase in rate of weight gain, as an aid in the prevention of coccidiosis caused by Eimeria necatrix, E tenella, E acervulina, E maxima, E brunetti, and E. mivati	C	Do not feed to laying chickens, feed continuously as the sole ration, withdraw 5 days before slaughter, as sole source of organic arsenic, as monensin sodium provided by No. 000986 in Sec. 510 600(c) of this chapter, as virginiamycin provided by No 066104 in Sec 510 600(c) of this chapter, roxarsone provided by Nos 046753 and 011526 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5-15 g/ton	Monensin	90-110 g/ton	355	(f)(1)(xxi)	Poultry	Revoke	Broiler chickens: For increase in rate of weight gain, as an aid in the prevention of coccidiosis caused by Eimeria necatrix, E tenella, E acervulina, E maxima, E brunetti, and E mivati	C	Do not feed to laying chickens, feed continuously as sole ration, as monensin sodium provided by No 000986 in Sec 510 600 of this chapter; virginiamycin provided by No 066104 in Sec 510 600 of this chapter
Lincomycin	Lincosamide	2-4 g/ton	Nicarbazin, narasin	27-45, 27-45 g/ton	366	(d)	Poultry	Revoke	Broiler chickens; prevention of coccidiosis caused by Eimeria tenella, E necatrix, E acervulina, E maxima, E brunetti, E mivati, for increased rate of weight gain and improved feed efficiency	C	Feed continuously as sole ration Withdraw 5 days before slaughter Do not allow turkeys, horses, or other equines access to formulations containing narasin Ingestion of narasin by these species has been fatal Do not feed to laying hens Do not allow rabbits, hamsters, guinea pigs, horses, or ruminants access to feeds containing lincomycin Ingestion by these species may result in severe gastrointestinal effects Narasin and nicarbazin as provided by 000986, lincomycin by 000009.
Lincomycin	Lincosamide	2 g/ton	Nicarbazin	113 5 g/ton	366	(d)	Poultry	Revoke	Broiler chickens, aid in preventing outbreaks of secal (Eimeria tenella) and intestinal (E acervulina, E maxima, E necatrix, and E brunetti) coccidiosis, for increased rate of weight gain	C	Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard, do not use as a treatment for coccidiosis, do not use in flushing mashes, do not feed to laying hens, withdraw 4 days before slaughter
Lincomycin	Lincosamide	2 g/ton	Nicarbazin, roxarsone	113 5, 22 7 g/ton	366	(d)	Poultry	Revoke	Broiler chickens, aid in preventing outbreaks of secal (Eimeria tenella) and intestinal (E acervulina, E maxima, E necatrix, and E brunetti) coccidiosis; for increased rate of weight gain	C	Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard, as sole source of organic arsenic, do not use a treatment or coccidiosis, do not use in flushing mashes, do not feed to laying hens, withdraw 5 days before slaughter.
Sulfanitran	Sulfonamide	272 g/ton	Nitromide	227 g/ton	376	ALL	Poultry	Revoke	As an aid in the prevention of coccidiosis caused by Eimeria tenella, E necatrix, and E acervulina	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter, from Type A articles containing not more than 25 percent nitromide and 30 percent sulfanitran

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Sulfanitran	Sulfonamide	272 g/ton	Nitromide, roxarsone	227, 45 4 g/ton	376	ALL	Poultry	Revoke	Prevention of coccidiosis caused by Eimena tenella, E necatrix, and E acervulina, growth promotion and feed efficiency, improving pigmentation	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter, from Type A articles containing not more than 25 percent nitromide, 30 per cent sulfanitan, and 5 percent roxarsone, as sole source of organic arsenic
Oleandomycin	Macrolide	1-2 g/ton			435	ALL	Poultry	Revoke	For increased rate of weight gain and improved feed efficiency for broiler chickens and growing turkeys	NS	
Oxytetracycline	Tetracycline	10-50 g/ton			450	(d)(1)(ii)	Poultry	Revoke	1 Chickens, increased rate of weight gain and improved feed efficiency	NS	Do not feed to chickens producing eggs for human consumption
Penicillin procaine	Penicillin	2.4-50 g/ton			460	(d)(1)(i)	Poultry	Revoke	Chickens, turkeys, and pheasants, for increased rate of weight gain and improved feed efficiency	NS	Do not feed to poultry producing eggs for human consumption
Chlortetracycline	Tetracycline	100-200 g/ton	Robenidine	30 g/ton	515	(d)	Poultry	Amend	For broiler and fryer chickens As an aid in the prevention of coccidiosis caused by E mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix For control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	14 days	Feed continuously as sole ration up to 14 days Do not feed to chickens producing eggs for human consumption Withdraw 5 days prior to slaughter.
Chlortetracycline	Tetracycline	200-400 g/ton	Robenidine	30 g/ton	515	(d)	Poultry	Amend	For broiler and fryer chickens As an aid in the prevention of coccidiosis caused by E mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix For control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and E coli susceptible to chlortetracycline	14 days	Feed continuously as sole ration up to 14 days. Do not feed to chickens producing eggs for human consumption Withdraw 5 days prior to slaughter
Chlortetracycline	Tetracycline	500 g/ton	Robenidine	30 g/ton	515	(d)	Poultry	Amend	For broiler and fryer chickens As an aid in the prevention of coccidiosis caused by E mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix As an aid in the reduction of mortality due to E coli susceptible to chlortetracycline	5 days	Feed continuously as sole ration up to 5 days. Do not feed to chickens producing eggs for human consumption Withdraw 5 days prior to slaughter
Lincomycin	Lincosamide	2 g/ton	Robenidine	30 g/ton	515	(d)	Poultry	Revoke	For broiler and fryer chickens As an aid in the prevention of coccidiosis caused by E mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix For increase in rate of weight gain and improved feed efficiency	C	Feed continuously as the sole ration. Do not feed to laying hens Withdraw 5 days before slaughter
Oxytetracycline	Tetracycline	400 g/ton	Robenidine	30 g/ton	515	(d)	Poultry	Amend	For broiler and fryer chickens As an aid in the prevention of coccidiosis caused by E mivati, E brunetti, E tenella, E acervulina, E maxima, and E necatrix For control of CRD and air sac infection caused by Mycoplasma allisepticum and E coli susceptible to oxytetracycline	14 days	Feed continuously as sole ration up to 14 days Do not feed to chickens producing eggs for human consumption Withdraw 5 days prior to slaughter.
Chlortetracycline	Tetracycline	10-50 g/ton	Roxarsone	22.7-45 4 g/ton	530	(d)(2)(i)	Poultry	Revoke	For increased rate of weight gain, improved feed efficiency, and improved pigmentation	NS	Do not feed to chickens producing eggs for human consumption, withdraw 5 days before slaughter, as sole source of organic arsenic, drug overdose or lack of water may result in leg weakness, feed continuously throughout growing period
Chlortetracycline	Tetracycline	100-200 g/ton	Roxarsone	22.7-45 4 g/ton	530	(d)(2)(ii)	Poultry	Amend	For increased rate of weight gain, improved feed efficiency, and improved pigmentation, control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption, withdraw 5 days before slaughter, as sole source of organic arsenic, drug overdose or lack of water may result in leg weakness, feed continuously for 7 to 14 days
Chlortetracycline	Tetracycline	200-400 g/ton	Roxarsone	22 7-45 4 g/ton	530	(d)(2)(iii)	Poultry	Amend	For increased rate of weight gain, improved feed efficiency, and improved pigmentation, control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and Escherichia coli susceptible to chlortetracycline.	7-14 days	Do not feed to chickens producing eggs for human consumption, withdraw 5 days before slaughter, as sole source of organic arsenic, drug overdose or lack of water may result in leg weakness, feed continuously for 7 to 14 days
Chlortetracycline	Tetracycline	500 g/ton	Roxarsone	22 7-45 4 g/ton	530	(d)(2)(iv)	Poultry	Amend	For increased rate of weight gain, improved feed efficiency, and improved pigmentation, reduction of mortality due to E coli infections susceptible to chlortetracycline	5 days	Do not feed to chickens producing eggs for human consumption; withdraw 5 days before slaughter, as sole source of organic arsenic, drug overdose or lack of water may result in leg weakness, feed continuously for 5 days
Chlortetracycline	Tetracycline	500 g/ton	Salinomycin, roxarsone	40-60, 45.4 g/ton	550	(d)(1)(xv)	Poultry	Amend	For prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E maxima, E brunetti, and E mivati, including some field strains of E tenella which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone, and as an aid in the reduction of mortality due to E coli infections susceptible to such treatment	5 days	Do not feed to layers In feeds containing 0 8 percent dietary calcium, not to be fed for more than 5 days Not approved for use with pellet binders Withdraw 5 days before slaughter May be fatal if accidentally fed to adult turkeys or to horses

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	500 g/ton	Salinomycin	40-60 g/ton	550	(d)(1)(xvi)	Poultry	Amend	For prevention of coccidiosis caused by Eimena tenella, E. necatrix, E acervulina, E maxima, E brunetti, and E mivati, and as an aid in the reduction of mortality due to E. coli infections susceptible to such treatment	5 days	Do not feed to layers In feeds containing 0 8 percent dietary calcium Not to be fed for more than 5 days Not approved for use with pellet binders Withdraw 24 hours before slaughter May be fatal if accidentally fed to adult turkeys or horses
Lincomycin	Lincosamide	2-4 g/ton	Salinomycin	40-60 g/ton	550	(d)(1)(xiii)	Poultry	Revoke	Broilers For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E maxima, E brunetti, and E mivati and for improved feed efficiency	C	Feed continuously as sole ration Not approved for use with pellet binders Do not feed to layers Do not allow horses, adult turkeys, guinea pigs, rabbits, hamsters, or ruminants access to this feed Ingestion by these species may result in severe gastrointestinal effects or may be fatal Lincomycin hydrochloride monohydrate as provided by No 000009 in Sec 510 600(c) of this chapter
Lincomycin	Lincosamide	2 g/ton	Salinomycin, roxarsone	40-60, 45 4 g/ton	550	(d)(1)(xiv)	Poultry	Revoke	Broilers For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E. maxima, E. brunetti, and E mivati, including some field strains of E tenella that are more susceptible to roxarsone combined with salinomycin than to salinomycin alone, and for improved feed efficiency	C	Feed continuously as sole ration Not approved for use with pellet binders Drug overdose or lack of water may result in leg weakness Do not feed to layers Do not allow horses, adult turkeys, guinea pigs, rabbits, hamsters, or ruminants access to this feed Ingestion by these species may result in severe gastrointestinal effects or may be fatal Withdraw 5 days before slaughter Lincomycin hydrochloride monohydrate as provided by No 000009 in Sec 510.600(c) of this chapter Roxarsone as provided by No Alpharma in Sec 510 600(c) of this chapter.
Tylosin	Macrolide	4-50 g/ton	Salinomycin	40-60 g/ton	550	(d)(1)(xxii)	Poultry	Revoke	Broilers. As an aid in the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E maxima, E brunetti, and E. mivati, and for increased rate of weight gain and improved feed efficiency	C	For broiler chickens only Feed continuously as sole ration Do not feed to laying hens Not approved for use with pellet binders May be fatal if accidentally fed to adult turkeys or horses Salinomycin as provided by Alpharma, tylosin phosphate as provided by 000986 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5 g/ton	Salinomycin	40-60 g/ton	550	(d)(1)(x)	Poultry	Revoke	Broilers For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E. maxima, E brunetti, and E. mivati, and for increased rate of weight gain and improved feed efficiency	C	Feed continuously as sole ration Not approved for use with pellet binders Do not feed to layers or to chickens over 16 weeks of age. May be fatal if accidentally fed to adult turkeys or horses Virginiamycin as provided by No 066104 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5-15 g/ton	Salinomycin	40-60 g/ton	550	(d)(1)(xi)	Poultry	Revoke	Broilers For the prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E maxima, E. brunetti, and E. mivati, and for increased rate of weight gain	C	Feed continuously as sole ration Not approved for use with pellet binders Do not feed to layers or to chickens over 16 weeks of age. May be fatal if accidentally fed to adult turkeys or horses Virginiamycin as provided by No 066104 in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	5 g/ton	Salinomycin, roxarsone	40-60, 45.4 g/ton	550	(d)(1)(xii)	Poultry	Revoke	Broilers For prevention of coccidiosis caused by Eimena tenella, E necatrix, E acervulina, E maxima, E. brunetti, and E mivati, including some field strains of E tenella which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone, and for improved feed efficiency.	C	Feed continuously as sole ration Withdraw 5 days prior to slaughter Use as sole source of organic arsenic Not approved for use with pellet binders Do not feed to layers May be fatal if accidentally fed to adult turkeys or horses Virginiamycin as provided by No 066104 in Sec 510 600(c) of this chapter. Roxarsone as provided by No Alpharma in Sec 510 600(c) of this chapter
Virginiamycin	Streptogramin	20 g/ton	Semduramicin	22 7 g/ton	555	(d)(5)	Poultry	Amend	Broiler chickens: For the prevention of coccidiosis caused by Eimena tenella, E acervulina, E maxima, E brunetti, E necatrix, and E mivati/mitis, and for prevention of necrotic enteritis caused by Clostridium perfringens susceptible to virginiamycin	C	For broiler chickens only Feed continuously as sole ration Do not feed to laying hens
Virginiamycin	Streptogramin	5-15 g/ton	Semduramicin	22 7 g/ton	555	(d)(6)	Poultry	Revoke	Broiler chickens: For the prevention of coccidiosis caused by Eimena tenella, E acervulina, E maxima, E brunetti, E necatrix, and E mivati/mitis, and for increased rate of weight gain	C	For broiler chickens only Feed continuously as sole ration Do not feed to laying hens

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Virginiamycin	Streptogramin	5 g/ton	Semduramicin	22 7 g/ton	555	(d)(7)	Poultry	Revoke	Broiler chickens For the prevention of coccidiosis caused by Eimeria tenella, E acervulina, E maxima, E brunetti, E necatrix, and E mivati/mitis, and for increased rate of weight gain and improved feed efficiency.	C	For broiler chickens only Feed continuously as sole ration Do not feed to laying hens
Virginiamycin	Streptogramin	20 g/ton	Semduramicin, roxarsone	22 7, 22 7-45 4 g/ton	555	(d)(8)	Poultry	Amend	Broiler chickens For the prevention of coccidiosis caused by Eimeria tenella, E acervulina, E maxima, E brunetti, E necatrix, and E mivati/mitis, for prevention of necrotic enteritis caused by Clostridium perfringens susceptible to virginiamycin, and for increased rate of weight gain, improved feed efficiency, and improved pigmentation	C	Feed continuously as sole ration throughout growing period Withdraw 5 days before slaughter For broiler chickens only. Do not feed to laying hens Use as sole source of organic arsenic. Poultry should have access to drinking water at all times Drug overdose or lack of water may result in leg weakness
Sulfadimethoxine	Sulfonamide	113.5 g/ton	Ormetoprim	68.1 g/ton	575	(d)(1)(i)	Poultry	Revoke	Broiler chickens As an aid in the prevention of coccidiosis caused by all Eimeria species known to be pathogenic to chickens, namely, E tenella, E necatrix, E acervulina, E brunetti, E mivati, and E maxima, and bacterial infections due to H gallinarum (infectious coryza), E coli (colibacillosis) and P multocida (fowl cholera)	NS	Feed as sole ration, withdraw 5 days before slaughter
Sulfadimethoxine	Sulfonamide	113 5 g/ton	Ormetoprim, roxarsone	68 1, 22 7 g/ton	575	(d)(1)(ii)	Poultry	Amend	Broiler chickens As an aid in the prevention of coccidiosis caused by all Eimeria species known to be pathogenic to chickens, namely E tenella, E necatrix, E acervulina, E brunetti, E. mivati, and E maxima, and bacterial infections due to H gallinarum (infectious coryza), E coli, (colibacillosis), and P multocida (fowl cholera), growth promotion and feed efficiency, improving pigmentation	NS	Withdraw 5 days before slaughter; as sole source of organic arsenic
Sulfadimethoxine	Sulfonamide	113 5 g/ton	Ormetoprim	68 1 g/ton	575	(d)(2)	Poultry	Amend	Replacement chickens As an aid in the prevention of coccidiosis caused by all Eimeria species known to be pathogenic to chickens, namely E tenella, E necatrix, E acervulina, E brunetti, E mivati, and E maxima, and bacterial infections due to H galmaxima, and bacterial infections due to H gallinarum (infectious coryza), E coli (colibacillosis) and P multocida (fowl cholera)	NS	Feed as a sole ration, do not feed to chickens over 16 weeks (112 days) of age, withdraw 5 days before slaughter
Sulfaquinoxoline	Sulfonamide	0 015%			586	(f)(1)(i)	Poultry	Revoke	Chickens As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E necatrix, E acervulina, E maxima, and E brunetti under average conditions of exposure	C	Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard If death losses exceed 0 5 percent in a 2-day period, obtain a laboratory diagnosis If coccidiosis is the cause, use the sulfaquinoxaline levels recommended for control of outbreaks, returning to the original dosage schedule after the outbreak has subsided Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions. Do not treat chickens within 10 days of slaughter Do not medicate chickens producing eggs for human consumption
Sulfaquinoxoline	Sulfonamide	0 0175%			586	(f)(1)(ii)	Poultry	Revoke	Chickens As an aid in preventing outbreaks of coccidiosis caused by Eimeria tenella, E necatrix, E acervulina, E maxima, and E brunetti where excessive exposure to coccidia is increased due to overcrowding or other management factors	C	Feed continuously from the time birds are placed on litter and continue past the age when coccidiosis is ordinarily a hazard If death losses exceed 0 5 percent in a 2-day period, obtain a laboratory diagnosis If coccidiosis is the cause, use the sulfaquinoxaline levels recommended for control of outbreaks, returning to the original dosage schedule after the outbreak has subsided Losses may result from intercurrent disease, other conditions affecting drug intake, or variant strains of coccidia species which can contribute to the virulence of coccidiosis under field conditions Do not treat chickens within 10 days of slaughter Do not medicate chickens producing eggs for human consumption
Tylosin	Macrolide	4-50 g/ton			625	(f)(1)(iii)	Poultry	Revoke	Chickens For increased rate of weight gain and improved feed efficiency	NS	As tylosin phosphate

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Virginiamycin	Streptogramin	5-15 g/ton			635	(d)(2)(i)	Poultry	Revoke	For increased rate of weight gain, for use in broiler chickens, not for use in layers	NS	Not for use in layers
Virginiamycin	Streptogramin	5 g/ton			635	(d)(2)(ii)	Poultry	Revoke	For increased rate of weight gain and improved feed efficiency in broiler chickens, not for use in layers.	NS	Not for use in layers
Virginiamycin	Streptogramin	20 g/ton			635	(d)(2)(iii)	Poultry	Amend	For prevention of necrotic enteritis caused by Clostridium perfringens susceptible to virginiamycin in broiler chickens, not for use in layers	NS	Not for use in layers
Chlortetracycline	Tetracycline	100-200 g/ton	Zoalene	36.3-113 5 g/ton	680	(d)(1)(i)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, control of infectious synovitis caused by Mycoplasma synoviae susceptible to chlortetracycline	NS	Do not feed to chickens producing eggs for human consumption, grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i)
Chlortetracycline	Tetracycline	200-400 g/ton	Zoalene	36.3-113.5 g/ton	680	(d)(1)(i)	Poultry	Amend	Replacement chickens, development of active immunity to coccidiosis, control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and Escherichia coli susceptible to chlortetracycline	NS	Do not feed to chickens producing eggs for human consumption, grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i).
Chlortetracycline	Tetracycline	100-200 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Amend	Broiler chickens, prevention and control of coccidiosis, control of infectious synovitis caused by M synoviae susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption, feed continuously for 7 to 14 d
Chlortetracycline	Tetracycline	200-400 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Amend	Broiler chickens, prevention and control of coccidiosis, control of chronic respiratory disease (CRD) and air sac infection caused by M gallisepticum and E coli susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption, feed continuously for 7 to 14 d
Erythromycin	Macrolide	4.6-18.5 g/ton	Zoalene, arsanilic acid	36 3-113 5, 90 g/ton	680	(d)(1)(i)	Poultry	Revoke	Replacement chickens, growth promotion and feed efficiency, development of active immunity coccidiosis, improving pigmentation	NS	As erythromycin thiocyanate, grower ration not to be fed to birds over 14 weeks of age, withdraw 5 d before slaughter, as sole source of organic arsenic, feed as in subtable item (i)
Erythromycin	Macrolide	92.5 g/ton	Zoalene, arsanilic acid	36.3-113 5, 90 g/ton	680	(d)(1)(i)(1)	Poultry	Amend	Replacement chickens, as an aid in the prevention of chronic respiratory disease during periods of stress, development of active immunity to coccidiosis, growth promotion and feed efficiency, improving pigmentation	5-8 days	Feed for 2 d before stress and 3 to 6 d after stress, as erythromycin thiocyanate, grower ration not to be fed to birds over 14 weeks of age, withdraw 5 d before slaughter, as sole source of organic arsenic arsenic, feed as in subtable in item (i)
Erythromycin	Macrolide	92.5 g/ton	Zoalene, arsanilic acid	36 3-113 5, 90 g/ton	680	(d)(1)(i)(2)	Poultry	Amend	Replacement chickens, as an aid in the prevention of infectious coryza, development of active immunity to coccidiosis, growth promotion and feed efficiency, improving pigmentation	7-14 days	Feed for 7 to 14 d, as erythromycin thiocyanate, grower ration not to be fed to birds over 14 weeks of age, withdraw 5 d before slaughter, as sole source of organic arsenic, feed as in subtable in item (i)
Erythromycin	Macrolide	185 g/ton	Zoalene, arsanilic acid	36 3-113.5, 90 g/ton	680	(d)(1)(i)	Poultry	Amend	Replacement chickens, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, growth promotion and feed efficiency, improving pigmentation and development of active immunity to coccidiosis	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 5 d before slaughter, as erythromycin thiocyanate, as sole source of organic arsenic, feed as in subtable in item (i).
Erythromycin	Macrolide	4.6-18 5 g/ton	Zoalene	36 3-113.5 g/ton	680	(d)(1)(i)	Poultry	Revoke	Replacement chickens; growth promotion and feed efficiency; development of active immunity coccidiosis	NS	As erythromycin thiocyanate, grower ration not to be fed to birds over 14 weeks of age; feed as in subtable in item (i).
Erythromycin	Macrolide	92.5 g/ton	Zoalene	36.3-113 5 g/ton	680	(d)(1)(i)	Poultry	Amend	1 Replacement chickens, as an aid in the prevention of chronic respiratory disease during periods of stress, development of active immunity to coccidiosis 2 Replacement chickens, as an aid in the prevention of infectious coryza, development of active immunity to coccidiosis	5-14 days	1 Feed for 2 d before stress and 3 to 6 after stress; withdraw 24 hours (h) before slaughter, as erythromycin thiocyanate, grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i) 2 Feed for 7 to 14 d, withdraw 24 h before slaughter, as erythromycin thiocyanate; grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i).
Erythromycin	Macrolide	185 g/ton	Zoalene	36 3-113 5 g/ton	680	(d)(1)(i)	Poultry	Amend	Replacement chickens, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, development of active immunity to coccidiosis	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 48 h before slaughter, grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i)
Erythromycin	Macrolide	4 6-18 5 g/ton	Zoalene, arsanilic acid	36.3-113 5, 90 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, growth prevention and control of coccidiosis, improving pigmentation	NS	As erythromycin thiocyanate; withdraw 5 d before slaughter; as sole source of organic arsenic

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Erythromycin	Macrolide	92 5 g/ton	Zoalene, arsanilic acid	36 3-113 5, 90 g/ton	680	(d)(1)(ii)	Poultry	Amend	1 Broiler chickens, as an aid in the prevention of chronic respiratory disease during stress, growth promotion and feed efficiency; improving pigmentation, control of coccidiosis. 2 Broiler chickens, prevention and control of coccidiosis, growth promotion and feed efficiency, improving pigmentation, as an aid in the prevention of infectious coryza	NS	As erythromycin thiocyanate; withdraw 5 d before slaughter; as sole source of organic arsenic
Erythromycin	Macrolide	185 g/ton	Zoalene, arsanilic acid	36.3-113.5, 90 g/ton	680	(d)(1)(ii)	Poultry	Amend	Broiler chickens; as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, prevention and control of coccidiosis, growth promotion and feed efficiency, improving pigmentation	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, as erythromycin thiocyanate, withdraw 5 d before slaughter, as sole source of organic arsenic
Erythromycin	Macrolide	4 6-18 5 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens; growth promotion and feed efficiency, prevention and control of coccidiosis	NS	As erythromycin thiocyanate
Erythromycin	Macrolide	92.5 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Amend	1 Broiler chickens, as an aid in the prevention of chronic respiratory disease during periods of stress, prevention and control of coccidiosis 2 Broiler chickens, as an aid in the prevention of infectious coryza, prevention and control of coccidiosis	5-14 days	1 Feed for 2 d before stress and 3 to 6 after stress, withdraw 24 h before slaughter, as erythromycin thiocyanate 2 Feed for 7 to 14 d, withdraw 24 h before slaughter, as erythromycin thiocyanate
Erythromycin	Macrolide	185 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Amend	Broiler chickens, as an aid in the prevention and reduction of lesions and in lowering severity of chronic respiratory disease, prevention and control of coccidiosis	5-8 days	Feed for 5 to 8 d, do not use in birds producing eggs for food purposes, withdraw 48 h before slaughter, as erythromycin thiocyanate
Lincomycin	Lincosamide	2 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, increase in rate of weight gain, improved feed efficiency, as an aid in the prevention and control of coccidiosis.	NS	Do not feed to laying chickens, to be fed as the sole ration; as lincomycin hydrochloride monohydrate
Penicillin procaine	Penicillin	2 4-50 g/ton	Zoalene, arsanilic acid	36.3-113.5, 90 g/ton	680	(d)(1)(i)	Poultry	Revoke	Replacement chickens, growth promotion and feed efficiency, development of active immunity to coccidiosis, improving pigmentation	NS	As procaine penicillin, grower ration not to be fed to birds over 14 weeks of age, withdraw 5 d before slaughter; as sole source of organic arsenic, feed as in subtable in item (i)
Penicillin procaine	Penicillin	2 4-50 g/ton	Zoalene	36.3-113 5 g/ton	680	(d)(1)(i)	Poultry	Revoke	Replacement chickens, growth promotion and feed efficiency, development of active immunity to coccidiosis	NS	As procaine penicillin, grower ration not to be fed to birds over 14 weeks of age, feed as in subtable in item (i)
Penicillin procaine	Penicillin	2 4-50 g/ton	Zoalene, roxarsone	36 3-113.5, 22.7-45.4 g/ton	680	(d)(1)(i)	Poultry	Revoke	Replacement chickens, growth promotion and feed efficiency, development of active immunity to coccidiosis, improving pigmentation	NS	As procaine penicillin, grower ration not to be fed to birds over 14 weeks of age, withdraw 5 d before slaughter, as sole source of organic arsenic, feed as in subtable in item (i)
Penicillin procaine	Penicillin	2.4-50 g/ton	Zoalene, arsanilic acid	36 3-113 5, 90 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, growth promotion and feed efficiency, prevention and control of coccidiosis, improving pigmentation	NS	As procaine penicillin, withdraw 5 d before slaughter, as sole source of organic arsenic
Penicillin procaine	Penicillin	2.4-50 g/ton	Zoalene	113 5 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, growth promotion and feed efficiency, prevention and control of coccidiosis	NS	As procaine penicillin
Penicillin procaine	Penicillin	2 4-50 g/ton	Zoalene, roxarsone	113 5, 22 7-45 4 g/ton	680	(d)(1)(ii)	Poultry	Revoke	Broiler chickens, prevention and control of coccidiosis, growth promotion and feed efficiency, improving pigmentation	NS	Withdraw 5 d before slaughter, as sole source of organic arsenic, as procaine penicillin
Chlortetracycline	Tetracycline	400 g/ton	Bacitracin methylene disalicylate	10-30 g/ton	76	(d)(1)(iv)	Swine	Amend	Swine, for increased rate of weight gain and improved feed efficiency, for treatment of bacterial enteritis caused by Escherichia coli and Salmonella choleraesuis and bacterial pneumonia caused by Pasteurella multocida susceptible to chlortetracycline	14 days	Feed for not more than 14 days to provide 10 milligrams of chlortetracycline per pound of body weight per day, as chlortetracycline provided by No Alpharma in Sec 510.600(c) of this chapter Type C feed may be prepared from Type B feed containing 1 to 3 grams per pound BMD with 400 grams per pound CTC, to Alpharma in Sec. 510 600(c)
Chlortetracycline	Tetracycline	400 g/ton	Bacitracin methylene disalicylate	10-30 g/ton	76	(d)(1)(iv)	Swine	Amend	Swine, for control of porcine proliferative enteropathies (ileitis) caused by Lawsonia intracellularis susceptible to chlortetracycline	14 days	Feed for not more than 14 days, chlortetracycline and BMD[reg] as provided by 046573 in Sec 510 600(c) of this chapter
Oxytetracycline	Tetracycline	10 mg/lb bw	Carbadox	10-25 g/ton	115	None***	Swine	Amend	For treatment of bacterial enteritis caused by Escherichia coli and S choleraesuis susceptible to oxytetracycline, for treatment of bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline, and for increased rate of weight gain and improved feed efficiency	7-14 days	Feed continuously for 7 to 14 days Not for use in pregnant swine or swine intended for breeding purposes Do not feed to swine within 42 days of slaughter
Chlortetracycline	Tetracycline	10-50 g/ton			128	(e)(3)(i)	Swine	Revoke	Growing swine For increased rate of weight gain and improved feed efficiency	NS	
Chlortetracycline	Tetracycline	50-100 g/ton			128	(e)(3)(ii)	Swine	Revoke	Swine For reducing the incidence of cervical lymphadenitis (jowl abscesses) caused by Group E Streptococci susceptible to chlortetracycline	NS	

Drug	Class	Dose	Combination drug(s)	Dose	21CFR§§ subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	400 g/ton			128	(e)(3)(iii)	Swine	Amend	Breeding swine For the control of leptospirosis (reducing the incidence of abortion and shedding of leptospirae) caused by Leptospira pomona susceptible to chlortetracycline	7-14 days	Feed continuously for no more than 14 d
Chlortetracycline	Tetracycline	100 g/ton	Procaine penicillin, sulfamethazine	50, 100 g/ton	145	ALL	Swine	Amend	It is administered to swine in a Type C feed for reduction of the incidence of cervical abscesses, treatment of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by Salmonella choleraesuis and vibrionic dysentery), prevention of these diseases during times of stress, maintenance of weight gains in the presence of atrophic rhinitis, growth promotion and increased feed efficiency in swine weighing up to 75 pounds	NS	Withdraw 15 days prior to slaughter
Chlortetracycline	Tetracycline	100 g/ton	Sulfathiazole, penicillin	100, 50 g/ton	155	ALL	Swine	Amend	For reduction of incidence of cervical abscesses Treatment of bacterial enteritis (salmonellosis or necrotic enteritis caused by Salmonella choleraesuis and vibrionic dysentery) Maintenance of weight gains in the presence of atrophic rhinitis Swine 10 pounds of body weight to 6 weeks post-weaning Increased rate of weight gain and improved feed efficiency Swine 6 to 16 weeks post-weaning Increased rate of weight gain	NS	For swine raised in confinement (dry-lot) or on limited pasture Feed as sole ration. Withdraw 7 days prior to slaughter
Erythromycin	Macrolide	9 25-64 75 g/ton			248	(d)(1)(iii)	Swine	Revoke	Swine, increase in weight gain, improved feed efficiency in starter pigs (9 25 to 64 75) and grower-finishing pigs (9 25)	NS	Starter ration for animals up to 35 lb body weight
Chlortetracycline	Tetracycline	400 g/ton	Hygromycin B	12 g/ton	274	(c)(1)(ii)	Swine	Amend	Swine, control of infestation of large roundworms (Ascaris suis), nodular worms (Oesophagostomum dentatum) and whipworms (Trichuris suis); treatment of bacterial enteritis caused by E coli and Salmonella choleraesuis and bacterial pneumonia caused by P multocida susceptible to chlortetracycline	NS	Withdraw 15 d before slaughter
Tylosin	Macrolide	10-100 g/ton	Hygromycin B	12 g/ton	274	(c)(1)(ii)	Swine	Amend	Swine Control of infestations of large roundworms (Ascaris suis), nodular worms (Oesophagostomum dentatum), and whipworms (Trichuris suis), growth promotion and feed efficiency	C	As tylosin phosphate, withdraw 15 days prior to slaughter, feed continuously as follows Animal wt (lbs) Up to 40 20 to 100\1\ 41 to 100 .20 to 40\1\ 101 to market wt 10 to 20\1\
Lincomycin	Lincosamide	20 g/ton	Ivermectin	2 72 g/ton	300	(d)(2)	Swine	Amend	For treatment and control of gastrointestinal roundworms (Ascaris suum, adults and fourth-stage larvae; Ascarops strongylina, adults, Hyostrongylus rubidus, adults and fourth-stage larvae, Oesophagostomum spp , adults and fourth-stage larvae), kidneyworms (Stephanurus dentatus, adults and fourth-stage larvae), lungworms (Metastrongylus spp , adults), lice (Haematopinus suis), and mange mites (Sarcoptes scabiei var suis) For increased rate of weight gain	7 days	For weaned, growing-finishing swine Feed as only feed for 7 consecutive days Withdraw 5 days before slaughter A separate feed containing 20 grams per ton lincomycin may be continued Not to be fed to swine that weigh more than 250 pounds Do not allow rabbits, hamsters, guinea pigs, horses, or ruminants access to feeds containing lincomycin Ingestion by these species may result in severe gastrointestinal effects. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism
Lincomycin	Lincosamide	20 g/ton			325	(d)(2)(i)	Swine	Revoke	Growing-finishing swine For increased rate of weight gain	NS	Feed as sole ration Not to be fed to swine that weigh more than 250 pounds (lb)
Lincomycin	Lincosamide	40 g/ton			325	(d)(2)(ii)	Swine	Amend	1 For control of swine dysentery 2 For control of porcine proliferative enteropathies (ileitis) caused by Lawsonia intracellularis	NS	1 Feed as sole ration, for use in swine on premises with a history of swine dysentery but where symptoms have not yet occurred, or following use of lincomycin at 100 grams (g)/ton for treatment of swine dysentery Not to be fed to swine that weigh more than 250 lb 2 Feed as sole ration, or following use of lincomycin at 100 g/ton for control of porcine proliferative enteropathies (ileitis) Not to be fed to swine that weigh more than 250 lb
Oleandomycin	Macrolide	5-11 25 g/ton			435	ALL	Swine	Revoke	For increased rate of weight gain and improved feed efficiency in growing-finishing swine	NS	
Oxytetracycline	Tetracycline	10-50 g/ton			450	(d)(1)(ii)	Swine	Revoke	Swine, increased rate of weight and improved feed efficiency	NS	
Penicillin procaine	Penicillin	10-50 g/ton			460	(d)(1)(iii)	Swine	Revoke	Swine, for increased rate of weight gain and improved feed efficiency	NS	

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Lincomycin	Lincosamide	40 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(vii)	Swine	Amend	For control of swine dysentery, aid in the prevention of migration and establishment of large roundworm (Ascaris suum) infections; aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections	NS	Feed as sole ration, for use in swine on premises with a history of swine dysentery but where symptoms have not yet occurred; not to be fed to swine that weigh more than 250 pounds, withdraw 6 days before slaughter Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Lincomycin	Lincosamide	100, 40 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(viii)	Swine	Amend	For treatment and control of swine dysentery, aid in the prevention of migration and establishment of large roundworm (Ascaris suum) infections, aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections	21+ days	Feed 100 grams per ton for 3 weeks or until signs of disease disappear, followed by 40 grams per ton, feed as sole ration; not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Lincomycin	Lincosamide	100 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(ix)	Swine	Amend	For treatment of swine dysentery, aid in the prevention of migration and establishment of large roundworm (Ascaris suum) infections, aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections	21+ days	Feed 100 grams per ton 3 weeks or until signs of disease disappear, followed by 40 grams per ton, feed as sole ration; not to be fed to swine that weigh more than 250 pounds, withdraw 6 days before slaughter Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Lincomycin	Lincosamide	100 or 40 g/ton	Pyrantel tartrate	800 g/ton	485	(e)(1)(xi)	Swine	Amend	For treatment and/or control of swine dysentery, for removal and control of large roundworm (Ascaris suum) and nodular worm (Oesophagostomum spp) infections	NS	As sole ration for a single therapeutic treatment in Type C feed, feed at the rate of 1 lb of feed per 40 lb of body weight for animals up to 200 lb, and 5 lb of feed per head for animals 200 lb or over, withdraw 24 hours prior to slaughter, for use in swine on premises with a history of swine dysentery but where symptoms have not yet occurred, or following use of lincomycin at 100 grams (g)/ton for treatment of swine dysentery Not to be fed to swine that weigh more than 250 lb
Lincomycin	Lincosamide	200 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(xii)	Swine	Amend	For the reduction in severity of swine mycoplasma pneumonia caused by Mycoplasma hyopneumoniae, aid in the prevention of migration and establishment of large roundworms (Ascaris suum) infections, aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections	21 days	Feed as sole ration for 21 days, not to be fed to swine that weigh more than 250 pounds; withdraw 6 days before slaughter, consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Tylosin	Macrolide	40-100 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(v)	Swine	Amend	For prevention of swine dysentery (vibrionic), aid in the prevention of migration and establishment of large roundworms (Ascaris suum) infections, aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections	21+ days	Use 100 grams tylosin per ton for at least 3 weeks followed by 40 grams tylosin per ton until market weight, withdraw 24 hours before slaughter Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Tylosin	Macrolide	40-100 g/ton	Pyrantel tartrate	96 g/ton	485	(e)(1)(vi)	Swine	Amend	Treatment and control of swine dysentery (vibrionic), aid in the prevention of migration and establishment of large roundworm (Ascaris suum) infections; aid in the prevention of establishment of nodular worm (Oesophagostomum spp) infections.	14-42 days	Administer tylosin in feed as tylosin phosphate after treatment with tylosin in drinking water as tylosin base, 0 25 grams per gallon in drinking water for 3 to 10 days, 40 to 100 grams tylosin per ton in feed for 2 to 6 weeks, withdraw 24 hours before slaughter Consult your veterinarian before feeding to severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism
Tylosin	Macrolide	40 g/ton	Ractopamine	4 5 g/ton	500	(e)(1)(ii)	Swine	Revoke	Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight; and for prevention of swine dysentery (vibrionic)	21+ days	Feed continuously as sole ration until market weight following the use of tylosin at 100 grams per ton (g/t) for at least 3 weeks

Drug	Class	Dose	Combination drug(s)	Dose	§ICFR§§ subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Tylosin	Macrolide	100 g/ton	Ractopamine	4 5 g/ton	500	(e)(1)(iii)	Swine	Revoke	1 Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight, and for prevention and/or control of porcine proliferative enteropathies (ileitis) associated with Lawsonia intracellulans 2 Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight; and or prevention of swine dysentery (vibrionic)	21+ days	Feed continuously as sole ration for 21 days Feed continuously as sole ration for at least 3 weeks followed by tylosin at 40 g/t until market weight
Tylosin	Macrolide	40 g/ton	Ractopamine	4 5-18 g/ton	500	(e)(1)(v)	Swine	Revoke	Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight, and for prevention of swine dysentery (vibrionic)	21+ days	Feed continuously as sole ration until market weight following the use of tylosin at 100 grams per ton (g/t) for at least 3 weeks
Tylosin	Macrolide	100 g/ton	Ractopamine	4 5-18 g/ton	500	(e)(1)(vi)	Swine	Revoke	1 Finishing swine Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight, and for prevention and/or control of porcine proliferative enteropathies (ileitis) associated with Lawsonia intracellulans 2 Finishing swine Finishing swine For increased rate of weight gain, improved feed efficiency, and increased carcass leanness in finishing swine fed a complete ration containing at least 16 percent crude protein from 150 lb (68 kg) to 240 lb (109 kg) body weight, and or prevention of swine dysentery (vibrionic)	21+ days	Feed continuously as sole ration for 21 days Feed continuously as sole ration for at least 3 weeks followed by tylosin at 40 g/t until market weight
Chlortetracycline	Tetracycline	400 g/ton	Roxarsone	22 7-45.4 g/ton	530	(d)(4)(ii)	Swine	Amend	For increased rate of weight gain and improved feed efficiency, treatment of bacterial enteritis caused by E coli and S choleraesuis and bacterial pneumonia caused by P multocida susceptible to chlortetracycline	14 days	Withdraw 5 days before slaughter, as sole source of organic arsenic, feed for not more than 14 days
Chlortetracycline	Tetracycline	10-50 g/ton	Roxarsone	181.5 g/ton	530	(d)(4)(iv)	Swine	Amend	For the treatment of swine dysentery, increased rate of weight gain and improved feed efficiency	6 days	Feed for not more than 6 consecutive days, if improvement is not observed, consult a veterinarian; withdraw 5 days before slaughter, as a sole source or organic arsenic, animals must consume enough medicated feed to provide a therapeutic dose
Tilmicosin	Macrolide	181-363 g/ton			618	ALL	Swine	Amend	For the control of swine respiratory disease associated with Actinobacillus pleuropneumoniae and Pasteurella multocida	21 days	Feed continuously as the sole ration for 21-day period, beginning approximately 7 days before an expected disease outbreak Feed containing tilmicosin shall not be fed to pigs for more than 21 days during each phase of production without ceasing administration for reevaluation of antimicrobial use by a licensed veterinarian before reinitiating a further course of therapy with an appropriate antimicrobial The safety of tilmicosin has not been established in pregnant swine or swine intended for breeding purposes. Do not allow horses or other equines access to feeds containing tilmicosin Withdraw 7 days before slaughter
Tylosin	Macrolide	10-100 g/ton			625	(f)(1)(vi)(a)	Swine	Revoke	For increased rate of weight gain and improved feed efficiency	C	As tylosin phosphate, continuous use as follows Grams per ton 20-100, prestarter or starter, 20-40, grower, 10-20, finisher
Tylosin	Macrolide	40-100 g/ton			625	(f)(1)(vi)(b)	Swine	Revoke	Prevention of swine dysentery (vibronic)	21+ days	Use 100 grams per ton for at least 3 weeks followed by 40 grams per ton until market weight, as tylosin phosphate
Tylosin	Macrolide	100 g/ton			625	(f)(1)(vi)(d)	Swine	Revoke	Maintaining weight gains and feed efficiency in presence of atrophic rhinitis	NS	As tylosin phosphate

Drug	Class	Dose	Combination drug(s)	Dose	21CFR558 subsection	Section	Animal	Action*	Indications	Usage Time**	Limitations
Tylosin	Macrolide	100 g/ton			625	(f)(1)(vi)(e)	Swine	Amend	Prevention and/or control of procine proliferative enteropathies (ileitis) associated with Lawsonia intracellulars	21 days	As tylosin phosphate, administer for 21 days
Tylosin	Macrolide	100 g/ton	Sulfamethazine	100 g/ton	630	(f)(2)(i)	Swine	Amend	*Maintaining weight gains and feed efficiency in the* presence of atrophic rhinitis, lowering the incidence and severity of Bordetella bronchiseptica rhinitis, prevention of swine dysentery (vibrionic), control of swine pneumonias caused by bacterial pathogens (P multocida and/or C pyogenes), for reducing the incidence of cervical lymphadenitis (jowl abscesses) caused by Group E Streptococci. Only the sulfamethazine portion of this combination is active in controlling jowl abscesses	NS	As tylosin phosphate, withdraw 15 days before slaughter
Tylosin	Macrolide	100 g/ton	Sulfamethazine	100 g/ton	630	(f)(2)(ii)	Swine	Amend	Maintaining weight gains and feed efficiency in the presence of atrophic rhinitis, lowering the incidence and severity of Bordetella bronchiseptica rhinitis, prevention of swine dysentery (vibrionic), control of swine pneumonias caused by bacterial pathogens (Pasteurella multocida and/or Corynebacterium pyogenes)	NS	As tylosin phosphate, withdraw 15 days before slaughter
Virginiamycin	Streptogramin	25 g/ton			635	(d)(1)(iii)	Swine	Revoke	As an aid in control of dysentery in swine up to 120 pounds For use in animals or on premises with a history of swine dysentery but where symptoms have not yet occurred	NS	
Virginiamycin	Streptogramin	5, 10 g/ton			635	(d)(1)(iv)	Swine	Revoke	10 grams per ton from weaning up to 120 pounds for increased rate of weight gain and improved feed efficiency, followed by 5 grams per ton to market weight for increased rate of weight gain and improved feed efficiency	C	For continuous use from weaning to market weight
Virginiamycin	Streptogramin	10, 5-10 g/ton			635	(d)(1)(v)	Swine	Revoke	10 grams per ton from weaning up to 120 pounds for increased rate of weight gain and improved feed efficiency, followed by 5 to 10 grams per ton to market weight for increased rate of weight gain	C	For continuous use from weaning to market weight

Non-therapeutic antimicrobial use in livestock drinking water (21 CFR 520)

Drug	Class	Dose	Combination drug(s)	Dose	21CFR520	Section	Animal	Action*	Indications	Usage Time**	Limitations
Chlortetracycline	Tetracycline	250 mg/gallon	Sulfamethazine	250 mg/gallon	445a	ALL	Swine	Amend	Prevention and treatment of bacterial enteritis, aid in the reduction of the incidence of cervical abscesses, *aid in the maintenance of weight gains in the presence* of bacterial enteritis and atrophic rhinitis	28 days	Not to be used for more than 28 consecutive days, withdraw 15 days before slaughter, as sole source of chlortetracycline and sulfonamide
Spectinomycin	Aminoglycoside	2 g/gallon			2123b	(e)(1)	Poultry	Amend	As an aid in the prevention or control of losses due to *CRD associated with M gallisepticum (PPLO)*	3+ days	It is administered in the drinking water of growing chickens at 2 grams of spectinomycin per gallon of water as the only source of drinking water for the first 3 *days of life and for 1 day following each vaccination* Do not administer within 5 days of slaughter Do not administer to laying chickens
Spectinomycin	Aminoglycoside	0 5 g/gallon			2123b	(e)(2)	Poultry	Revoke	For increased rate of weight gain and improved feed efficiency	3+ days	Administered for the first 3 days of life and for 1 day following each vaccination Do not administer to laying *chickens Do not administer within 5 days of slaughter*

* **"Amend" means (i) revoking use for weight gain, feed efficiency, or growth promotion, and (ii) restricting use for disease control or prevention to situations where there has been a diagnosed outbreak of bacterial disease in the building, house or feedlot, for a period not to exceed 14 days.**

** **C=fed continuously, NS=not specified**

*** **Indications added since the latest Green Book update (April 2004)**